# PCT

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



#### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:

C12N 15/12, C07K 14/47, C12N 15/10,
15/11

(43) International Publication Number: WO 99/06553

(43) International Publication Date: 11 February 1999 (11.02.99)

(21) International Application Number: PCT/IB98/01237

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ,

US

(71) Applicant (for all designated States except US): GENSET [FR/FR]; 24, rue Royale, F-75008 Paris (FR).

1 August 1997 (01.08.97)

(72) Inventors; and

(30) Priority Data:

08/905,051

(75) Inventors/Applicants (for US only): DUMAS MILNE ED-WARDS, Jean-Baptiste [FR/FR]; 8, rue Grégoire de Tours, F-75006 Paris (FR). DUCLERT, Aymeric [FR/FR]; 6 ter, rue Victorine, F-94100 Saint-Maur (FR). LACROIX, Bruno [FR/FR]; 9, route de Vourles, F-69230 Saint-Genis Laval (FR).

(74) Agents: MARTIN, Jean-Jacques et al.; Cabinet Regimbeau, 26, avenue Kléber, P-75116 Paris (FR). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report: 8 April 1999 (08.04.99)

(54) Title: 5' ESTs FOR SECRETED PROTEINS EXPRESSED IN VARIOUS TISSUES

(57) Abstract

The sequences of 5' ESTs derived from mRNAs encoding secreted proteins are disclosed. The 5' ESTs may be to obtain cDNAs and genomic DNAs corresponding to the 5' ESTs. The 5' ESTs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. Upstream regulatory sequences may also be obtained using the 5' ESTs. The 5' ESTs may also be used to design expression vectors and secretion vectors.

# FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	Prance	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
ΑZ	Azerbaijan	GB	United Kingdom	MC	Моласо	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece -		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IK	Ireland	· MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	<b>Tceland</b>	MW	Malawi	US	United States of America
CA	Canada	m	Italy	MX	Mexico	uz	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal	•	
CU	Cuba ·	KZ	Kazakstan	RO	Romania		
. CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	· SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EB	Estonia	LR	Liberia	SG	Singapore		

International Application No PCT/1B 98/01237

A. CLASSIFICATION OF SUBJECT MATTER C07K14/47 C12N15/11 IPC 6 C12N15/12 C12N15/10 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12N C07K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages Category \* 3-8, ADAMS M D ET AL: "INITIAL ASSESSMENT OF X 15-19, **HUMAN GENE DIVERSITY AND EXPRESSION** 21,24,27 PATTERNS BASED UPON 83 MILLION NUCLEOTIDES OF CDNA SEQUENCE" NATURE, vol. 377, no. SUPPL, 28 September 1995, pages 3-17, XP002069461 12-14. Y see the whole document 29-32, 35-37 -& DATABASE EMBL - EMEST14 Entry HSZZ87788, Acc.No. AA382642, 18 April 1997 ADAMS, M.D. ET AL.: "EST95896 Testis I Homo spaiens cDNA 5' end." XP002083842 see the whole document -& DATABASE EMBL - EMEST14 Entry HSZZ86710, Acc.No. AA381563, Patent family members are listed in annex. Further documents are dated in the continuation of box C. X X Special categories of cited documents : T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be conside filing date involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. other means \*P\* document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 0 8. 02 99 10 November 1998 **Authorized officer** Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Smalt, R Fax: (+31-70) 340-3016

Internal Application No PC7, IB 98/01237

tegory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	18 April 1997 ADAMS, M.D. ET AL.: "EST94680 ACtivated T-cell I Homo sapiens CDNA 5' end." XP002083843 see the whole document	
	EP 0 279 582 A (BAYLOR COLLEGE MEDICINE) 24 August 1988 see the whole document	12,13
	LIN Y ET AL: "INHIBITION OF NUCLEAR TRANSLOCATION OF TRANSCRIPTION FACTOR NF-KB BY A SYNTHETIC PEPTIDE CONTAINING A CELL MEMBRANE-PERMEABLE MOTIF AND NUCLEAR LOCALIZATION SEQUENCE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 24, 16 June 1995, pages 14255-14258, XP002050723 see the whole document	14
•	GREENWOOD M T ET AL: "Cloning of the gene encoding human somatostatin receptor 2: sequence analysis of the 5'-flanking promoter region" GENE, vol. 159, no. 2, 4 July 1995, page 291-292	29-32
4	XP004042228 see the whole document	33
<b>Y</b>	LOCKHART D J ET AL: "EXPRESSION MONITORING BY HYBRIDIZATION TO HIGH-DENSITY OLIGONUCLEOTIDE ARRAYS" BIO/TECHNOLOGY, vol. 14, no. 13, December 1996, pages 1675-1680, XP002022521 see the whole document	35-37
A	HEIJNE VON G.: "A new method for predicting signal sequence cleavage sites" NUCLEIC ACIDS RESEARCH, vol. 14, no. 11, 1986, pages 4683-4690, XP002053954 cited in the application	12
A	WO 96 34981 A (GENSET (FR); MERENKOVA IRENA NICOLAEVNA; DUMAS MILNE EDWARDS JEAN) 7 November 1996 cited in the application	
<b>A</b>	KATO S. ET AL.: "Construction of a human full-length cDNA bank" GENE, vol. 150, 1994, pages 243-250, XP002081364 cited in the application	
	-/	

Interm "anal Application No PC7 / IB 98/01237

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 625 572 A (KANAGAWA ACAD OF SCIENCE AND TECHNOL FOUNDATION (JP); KATO S; SEKINE S) 23 November 1994 cited in the application	
A	CARNINCI P. ET AL.: "High-efficiency full-length cDNA cloning by biotinylated CAP trapper" GENOMICS, vol. 37, no. 3, 1 November 1996, pages 327-336, XP002081729 cited in the application	
<b>A</b> .	WO 97 07198 A (GENETICS INSTITUTE INC (US); JACOBS K; MCCOY JM; KELLEHER K; CARLIN M) 27 February 1997	
A	TASHIRO K. ET AL.: "Signal sequence trap: a cloning strategy for secreted proteins and type I membrane proteins" SCIENCE, vol. 261, 30 July 1993, pages 600-603, XP000673204	
A	YOKOYAMA-KOBAYASHI M. ET AL.: "A signal sequence detection system using secreted protease activity as an indicator" GENE, vol. 163, 1995, pages 193-196, XP002053953	
P,X	DATABASE EMBL - EMEST3 Entry/Acc.No. AA805310., 16 February 1998 STRAUSBERG, R.: "oc15a05.s1 NCI_CGAP_GCB1 Homo spaiens cDNA clone IMAGE:1340912." XP002083844 see the whole document	3-8
	·	
·		

Inte. .ional application No. PCT/IB 98/01237

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.:     because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-37 partially (Invention 1. on continuation-sheet)
Remark on Protest  The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: Invention 1: claims 1-37 all partially

Nucleic acid comprising the sequence as in Seq.ID:38, complementary sequence, fragments, hybridizing sequences. Polypeptide comprising a signal peptide encoded by said nucleotide sequence. Vector encoding a fusion protein comprising said signal peptide. A method of directing the extracellular secretion of a polypeptide by means of said vector. Method of importing a polypeptide into a cell by means of said signal peptide. A method for making a cDNA encoding a secretory protein, partially encoded by said nucleotide sequence, corresponding cDNA. Polypeptide encoded by said nucleotide sequence, comprising a sequence as in Seq.ID:186, method of making said polypeptide. Method of obtaining a promoter located upstream of said nucleotide sequence, promoter thereof.

2. Claims: Inventions 2-147: claims 1-37 all partially

Inventions 2-147: Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:39-185, and corresponding polypeptides, where invention 2 is limited to Seq.ID:39 and 187, invention 3 is limited to Seq.ID:40 and 188,...., invention 147 is limited to Seq.ID:185 and 333).

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

ormation on patent family members

Inter onal Application No PC1/IB 98/01237

Patent document cited in search report		Publication date		ent family mber(s)	Publication date
EP 0279582	A	24-08-1988	AU AU AU CA EP JP US US	618524 B 1178488 A 661696 B 1941092 A 1321764 A 0832981 A 63309192 A 5565362 A 5304489 A	02-01-1992 18-08-1988 03-08-1995 24-09-1992 31-08-1993 01-04-1998 16-12-1988 15-10-1996 19-04-1994
WO 9634981	A	07-11-1996	FR FR AU CA EP	2733765 A 2733762 A 5982996 A 2220045 A 0824598 A	08-11-1996 08-11-1996 21-11-1996 07-11-1996 25-02-1996
EP 0625572	Α	23-11-1994	JP WO US	6153953 A 9408001 A 5597713 A	03-06-1994 14-04-1994 28-01-1997
WO 9707198	A	27-02-1997	US AU AU CA CA EP EP WO	5707829 A 6712396 A 6768596 A 2227220 A 2229208 A 0839196 A 0851875 A 9704097 A	13-01-1998 18-02-1997 12-03-1997 06-02-1997 27-02-1997 06-05-1998 08-07-1998

10

15

20

25

30

## 5' ESTs FOR SECRETED PROTEINS EXPRESSED IN VARIOUS TISSUES

## Background of the Invention

The estimated 50,000-100,000 genes scattered along the human chromosomes offer tremendous promise for the understanding, diagnosis, and treatment of human diseases. In addition, probes capable of specifically hybridizing to loci distributed throughout the human genome find applications in the construction of high resolution chromosome maps and in the identification of individuals.

In the past, the characterization of even a single human gene was a painstaking process, requiring years of effort. Recent developments in the areas of cloning vectors, DNA sequencing, and computer technology have merged to greatly accelerate the rate at which human genes can be isolated, sequenced, mapped, and characterized. Cloning vectors such as yeast artificial chromosomes (YACs) and bacterial artificial chromosomes (BACs) are able to accept DNA inserts ranging from 300 to 1000 kilobases (kb) or 100-400 kb in length respectively, thereby facilitating the manipulation and ordering of DNA sequences distributed over great distances on the human chromosomes. Automated DNA sequencing machines permit the rapid sequencing of human genes. Bioinformatics software enables the comparison of nucleic acid and protein sequences, thereby assisting in the characterization of human gene products.

Currently, two different approaches are being pursued for identifying and characterizing the genes distributed along the human genome. In one approach, large fragments of genomic DNA are isolated, cloned, and sequenced. Potential open reading frames in these genomic sequences are identified using bioinformatics software. However, this approach entails sequencing large stretches of human DNA which do not encode proteins in order to find the protein encoding sequences scattered throughout the genome. In addition to requiring extensive sequencing, the bioinformatics software may mischaracterize the genomic sequences obtained. Thus, the software may produce false positives in which non-coding DNA is mischaracterized as coding DNA or false negatives in which coding DNA is mislabeled as non-coding DNA.

An alternative approach takes a more direct route to identifying and characterizing human genes. In this approach, complementary DNAs (cDNAs) are synthesized from isolated messenger RNAs (mRNAs) which encode human proteins. Using this approach,

10

15

20

25

30

sequencing is only performed on DNA which is derived from protein coding portions of the genome. Often, only short stretches of the cDNAs are sequenced to obtain sequences called expressed sequence tags (ESTs). The ESTs may then be used to isolate or purify extended cDNAs which include sequences adjacent to the EST sequences. The extended cDNAs may contain all of the sequence of the EST which was used to obtain them or only a portion of the sequence of the EST which was used to obtain them. In addition, the extended cDNAs may contain the full coding sequence of the gene from which the EST was derived or, alternatively, the extended cDNAs may include portions of the coding sequence of the gene from which the EST was derived. It will be appreciated that there may be several extended cDNAs which include the EST sequence as a result of alternate splicing or the activity of alternative promoters.

In the past, these short EST sequences were often obtained from oligo-dT primed cDNA libraries. Accordingly, they mainly corresponded to the 3' untranslated region of the mRNA. In part, the prevalence of EST sequences derived from the 3' end of the mRNA is a result of the fact that typical techniques for obtaining cDNAs are not well suited for isolating cDNA sequences derived from the 5' ends of mRNAs. (Adams et al., Nature 377:3-174, 1996; Hillier et al., Genome Res. 6:807-828, 1996).

In addition, in those reported instances where longer cDNA sequences have been obtained, the reported sequences typically correspond to coding sequences and do not include the full 5' untranslated region of the mRNA from which the cDNA is derived. Such incomplete sequences may not include the first exon of the mRNA, particularly in situations where the first exon is short. Furthermore, they may not include some exons, often short ones, which are located upstream of splicing sites. Thus, there is a need to obtain sequences derived from the 5' ends of mRNAs.

While many sequences derived from human chromosomes have practical applications, approaches based on the identification and characterization of those chromosomal sequences which encode a protein product are particularly relevant to diagnostic and therapeutic uses. Of the 50,000-100,000 protein coding genes, those genes encoding proteins which are secreted from the cell in which they are synthesized, as well as the secreted proteins themselves, are particularly valuable as potential therapeutic agents. Such proteins are often

15.

20

25

30

involved in cell to cell communication and may be responsible for producing a clinically relevant response in their target cells.

In fact, several secretory proteins, including tissue plasminogen activator, G-CSF, GM-CSF, erythropoietin, human growth hormone, insulin, interferon-α, interferon-β, interferon-γ, and interleukin-2, are currently in clinical use. These proteins are used to treat a wide range of conditions, including acute myocardial infarction, acute ischemic stroke, anemia, diabetes, growth hormone deficiency, hepatitis, kidney carcinoma, chemotherapy induced neutropenia and multiple sclerosis. For these reasons, extended cDNAs encoding secreted proteins or portions thereof represent a particularly valuable source of therapeutic agents. Thus, there is a need for the identification and characterization of secreted proteins and the nucleic acids encoding them.

In addition to being therapeutically useful themselves, secretory proteins include short peptides, called signal peptides, at their amino termini which direct their secretion. These signal peptides are encoded by the signal sequences located at the 5' ends of the coding sequences of genes encoding secreted proteins. Because these signal peptides will direct the extracellular secretion of any protein to which they are operably linked, the signal sequences may be exploited to direct the efficient secretion of any protein by operably linking the signal sequences to a gene encoding the protein for which secretion is desired. In addition, portions of signal sequences may also be used to direct the intracellular import of a peptide or protein of interest. This may prove beneficial in gene therapy strategies in which it is desired to deliver a particular gene product to cells other than the cell in which it is produced. Signal sequences encoding signal peptides also find application in simplifying protein purification techniques. In such applications, the extracellular secretion of the desired protein greatly facilitates purification by reducing the number of undesired proteins from which the desired protein must be selected. Thus, there exists a need to identify and characterize the 5' portions of the genes for secretory proteins which encode signal peptides.

Public information on the number of human genes for which the promoters and upstream regulatory regions have been identified and characterized is quite limited. In part, this may be due to the difficulty of isolating such regulatory sequences. Upstream regulatory sequences such as transcription factor binding sites are typically too short to be utilized as probes for isolating promoters from human genomic libraries. Recently, some approaches

10

15

20

25

30

have been developed to isolate human promoters. One of them consists of making a CpG island library (Cross, et al., Nature Genetics 6: 236-244, 1994). The second consists of isolating human genomic DNA sequences containing SpeI binding sites by the use of SpeI binding protein. (Mortlock et al., Genome Res. 6:327-335, 1996). Both of these approaches have their limits due to a lack of specificity or of comprehensiveness.

The present 5' ESTs may be used to efficiently identify and isolate upstream regulatory regions which control the location, developmental stage, rate, and quantity of protein synthesis, as well as the stability of the mRNA. (Theil, *BioFactors* 4:87-93, 1993). Once identified and characterized, these regulatory regions may be utilized in gene therapy or protein purification schemes to obtain the desired amount and locations of protein synthesis or to inhibit, reduce, or prevent the synthesis of undesirable gene products.

In addition, ESTs containing the 5' ends of secretory protein genes may include sequences useful as probes for chromosome mapping and the identification of individuals. Thus, there is a need to identify and characterize the sequences upstream of the 5' coding sequences of genes encoding secretory proteins.

#### Summary of the Invention

The present invention relates to purified, isolated, or recombinant ESTs which include sequences derived from the authentic 5' ends of their corresponding mRNAs. The term "corresponding mRNA" refers to the mRNA which was the template for the cDNA synthesis which produced the 5' EST. These sequences will be referred to hereinafter as "5' ESTs." As used herein, the term "purified" does not require absolute purity; rather, it is intended as a relative definition. Individual 5' EST clones isolated from a cDNA library have been conventionally purified to electrophoretic homogeneity. The sequences obtained from these clones could not be obtained directly either from the library or from total human DNA. The cDNA clones are not naturally occurring as such, but rather are obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The conversion of mRNA into a cDNA library involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection. Thus, creating a cDNA library from messenger RNA and subsequently isolating individual clones from that library results in an approximately 10<sup>4</sup>-10<sup>6</sup> fold purification of the native message.

10

15

20

25

30

Purification of starting material or natural material to at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

As used herein, the term "isolated" requires that the material be removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide present in a living animal is not isolated, but the same polynucleotide, separated from some or all of the coexisting materials in the natural system, is isolated.

As used herein, the term "recombinant" means that the 5' EST is adjacent to "backbone" nucleic acid to which it is not adjacent in its natural environment. Additionally, to be "enriched" the 5' ESTs will represent 5% or more of the number of nucleic acid inserts in a population of nucleic acid backbone molecules. Backbone molecules according to the present invention include nucleic acids such as expression vectors, self-replicating nucleic acids, viruses, integrating nucleic acids, and other vectors or nucleic acids used to maintain or manipulate a nucleic acid insert of interest. Preferably, the enriched 5' ESTs represent 15% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. More preferably, the enriched 5' ESTs represent 50% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. In a highly preferred embodiment, the enriched 5' ESTs represent 90% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules.

"Stringent", moderate," and "low" hybridization conditions are as defined in Example 29.

Unless otherwise indicated, a "complementary" sequence is fully complementary.

Thus, 5' ESTs in cDNA libraries in which one or more 5' ESTs make up 5% or more of the number of nucleic acid inserts in the backbone molecules are "enriched recombinant 5' ESTs" as defined herein. Likewise, 5' ESTs in a population of plasmids in which one or more 5' EST of the present invention have been inserted such that they represent 5% or more of the number of inserts in the plasmid backbone are " enriched recombinant 5' ESTs" as defined herein. However, 5' ESTs in cDNA libraries in which 5' ESTs constitute less than 5% of the number of nucleic acid inserts in the population of backbone molecules, such as libraries in

10

15

20

25

30 .

which backbone molecules having a 5' EST insert are extremely rare, are not "enriched recombinant 5' ESTs."

In particular, the present invention relates to 5' ESTs which are derived from genes encoding secreted proteins. As used herein, a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal peptides in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g. soluble proteins), or partially (e.g. receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins which are transported across the membrane of the endoplasmic reticulum.

Such 5' ESTs include nucleic acid sequences, called signal sequences, which encode signal peptides which direct the extracellular secretion of the proteins encoded by the genes from which the 5' ESTs are derived. Generally, the signal peptides are located at the amino termini of secreted proteins.

Secreted proteins are translated by ribosomes associated with the "rough" endoplasmic reticulum. Generally, secreted proteins are co-translationally transferred to the membrane of the endoplasmic reticulum. Association of the ribosome with the endoplasmic reticulum during translation of secreted proteins is mediated by the signal peptide. The signal peptide is typically cleaved following its co-translational entry into the endoplasmic reticulum. After delivery to the endoplasmic reticulum, secreted proteins may proceed through the Golgi apparatus. In the Golgi apparatus, the proteins may undergo post-translational modification before entering secretory vesicles which transport them across the cell membrane.

The 5' ESTs of the present invention have several important applications. For example, they may be used to obtain and express cDNA clones which include the full protein coding sequences of the corresponding gene products, including the authentic translation start sites derived from the 5' ends of the coding sequences of the mRNAs from which the 5' ESTs are derived. These cDNAs will be referred to hereinafter as "full length cDNAs." These cDNAs may also include DNA derived from mRNA sequences upstream of the translation start site. The full length cDNA sequences may be used to express the proteins corresponding to the 5' ESTs. As discussed above, secreted proteins are therapeutically important. Thus, the proteins expressed from the cDNAs may be useful in treating or

10

15

20

25

30

controlling a variety of human conditions. The 5' ESTs may also be used to obtain the corresponding genomic DNA. The term "corresponding genomic DNA" refers to the genomic DNA which encodes the mRNA from which the 5' EST was derived.

Alternatively, the 5' ESTs may be used to obtain and express extended cDNAs encoding portions of the secreted protein. The portions may comprise the signal peptides of the secreted proteins or the mature proteins generated when the signal peptide is cleaved off. The portions may also comprise polypeptides having at least 10 consecutive amino acids encoded by the extended cDNAs or full length cDNAs. Alternatively, the portions may comprise at least 15 consecutive amino acids encoded by the extended cDNAs or full length cDNAs. In some embodiments, the portions may comprise at least 25 consecutive amino acids encoded by the extended cDNAs or full length cDNAs. In other embodiments, the portions may comprise at least 40 amino acids encoded by the extended cDNAs or full length cDNAs.

Antibodies which specifically recognize the entire secreted proteins encoded by the extended cDNAs, full length cDNAs, or fragments thereof having at least 10 consecutive amino acids, at least 15 consecutive amino acids, at least 25 consecutive amino acids, or at least 40 consecutive amino acids may also be obtained as described below. Antibodies which specifically recognize the mature protein generated when the signal peptide is cleaved may also be obtained as described below. Similarly, antibodies which specifically recognize the signal peptides encoded by the extended cDNAs or full length cDNAs may also be obtained.

In some embodiments, the extended cDNAs obtained using the 5' ESTs include the signal sequence. In other embodiments, the extended cDNAs obtained using the 5' ESTs may include the full coding sequence for the mature protein (i.e. the protein generated when the signal polypeptide is cleaved off). In addition, the extended cDNAs obtained using the 5' ESTs may include regulatory regions upstream of the translation start site or downstream of the stop codon which control the amount, location, or developmental stage of gene expression.

As discussed above, secreted proteins are therapeutically important. Thus, the proteins expressed from the extended cDNAs or full length cDNAs obtained using the 5' ESTs may be useful in treating or controlling a variety of human conditions.

10

15

20

25

The 5' ESTs (or cDNAs or genomic DNAs obtained therefrom) may be used in forensic procedures to identify individuals or in diagnostic procedures to identify individuals having genetic diseases resulting from abnormal expression of the genes corresponding to the 5' ESTs. In addition, the present invention is useful for constructing a high resolution map of the human chromosomes.

The present invention also relates to secretion vectors capable of directing the secretion of a protein of interest. Such vectors may be used in gene therapy strategies in which it is desired to produce a gene product in one cell which is to be delivered to another location in the body. Secretion vectors may also facilitate the purification of desired proteins.

The present invention also relates to expression vectors capable of directing the expression of an inserted gene in a desired spatial or temporal manner or at a desired level. Such vectors may include sequences upstream of the 5' ESTs, such as promoters or upstream regulatory sequences.

Finally, the present invention may also be used for gene therapy to control or treat genetic diseases. Signal peptides may also be fused to heterologous proteins to direct their extracellular secretion.

Bacterial clones containing Bluescript plasmids having inserts containing the 5' ESTs of the present invention (SEQ ID NOs: 38-185 are presently stored at 80°C in 4% (v/v) glycerol in the inventor's laboratories under the designations listed next to the SEQ ID NOs in II). The inserts may be recovered from the deposited materials by growing the appropriate clones on a suitable medium. The Bluescript DNA can then be isolated using plasmid isolation procedures familiar to those skilled in the art such as alkaline lysis minipreps or large scale alkaline lysis plasmid isolation procedures. If desired the plasmid DNA may be further enriched by centrifugation on a cesium chloride gradient, size exclusion chromatography, or anion exchange chromatography. The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the EST insertion. The PCR product which corresponds to the 5' EST can then be manipulated using standard cloning techniques familiar to those skilled in the art.

10

15

20

25

30

One aspect of the present invention is a purified or isolated nucleic acid having the sequence of one of SEQ ID NOs: 38-185 or having a sequence complementary thereto. In one embodiment, the nucleic acid is recombinant.

Another aspect of the present invention is a purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 38-185 or one of the sequences complementary thereto.

Yet another aspect of the present invention is a purified or isolated nucleic acid comprising at least 15 consecutive bases of one of the sequences of SEQ ID NOs: 38-185 or one of the sequences complementary thereto. In one embodiment, the nucleic acid is recombinant.

A further aspect of the present invention is a purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEQ ID NOs: 38-185 or one of the sequences complementary to the sequences of SEQ ID NOs: 38-185. In one embodiment, the nucleic acid is recombinant.

Another aspect of the present invention is a purified or isolated nucleic acid encoding a human gene product, said human gene product having a sequence partially encoded by one of the sequences of SEQ ID NO: 38-185.

Still another aspect of the present invention is a method of making a cDNA encoding a human secretory protein, said human secretory protein being partially encoded by one of SEQ ID NOs 38-185, comprising the steps of contacting a collection of mRNA molecules from human cells with a primer comprising at least 15 consecutive nucleotides of a sequence complementary to one of SEQ ID NOs: 38-185; hybridizing said primer to an mRNA in said collection that encodes said protein; reverse transcribing said hybridized primer to make a first cDNA strand from said mRNA; making a second cDNA strand complementary to said first cDNA strand; and isolating the resulting cDNA encoding said protein comprising said first cDNA strand and said second cDNA strand.

Another aspect of the invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method described in the preceding paragraph. In one embodiment, the

10

15

20

25

30

cDNA comprises the full protein coding sequence of said protein which sequence is partially included in one of the sequences of SEQ ID NOs: 38-185.

Another aspect of the present invention is a method of making a cDNA encoding a human secretory protein that is partially encoded by one of SEQ ID NOs 38-185, comprising the steps of obtaining a cDNA comprising one of the sequences of SEQ ID NOs: 38-185; contacting said cDNA with a detectable probe comprising at least 15 consecutive nucleotides of said sequence of SEQ ID NO: 38-185 or a sequence complementary thereto under conditions which permit said probe to hybridize to said cDNA; identifying a cDNA which hybridizes to said detectable probe; and isolating said cDNA which hybridizes to said probe.

Another aspect of the present invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method described in the preceding paragraph. In one embodiment, the cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-185.

Another aspect of the present invention is a method of making a cDNA comprising one of the sequence of SEQ ID NOs: 38-185, comprising the steps of contacting a collection of mRNA molecules from human cells with a first primer capable of hybridizing to the polyA tail of said mRNA; hybridizing said first primer to said polyA tail; reverse transcribing said mRNA to make a first cDNA strand; making a second cDNA strand complementary to said first cDNA strand using at least one primer comprising at least 15 nucleotides of one of the sequences of SEQ ID NOs 38-185; and isolating the resulting cDNA comprising said first cDNA strand and said second cDNA strand.

Another aspect of the present invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method described in the preceding paragraph. In one embodiment, the cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-185.

In one embodiment of the method described in the two paragraphs above, the second cDNA strand is made by contacting said first cDNA strand with a first pair of primers, said

10

15

20

25

30

first pair of primers comprising a second primer comprising at least 15 consecutive nucleotides of one of the sequences of SEQ ID NOs 38-185 and a third primer having a sequence therein which is included within the sequence of said first primer; performing a first polymerase chain reaction with said first pair of nested primers to generate a first PCR product; contacting said first PCR product with a second pair of primers, said second pair of primers comprising a fourth primer, said fourth primer comprising at least 15 consecutive nucleotides of said sequence of one of SEQ ID NOs: 38-185, and a fifth primer, said fourth and fifth primers being capable of hybridizing to sequences within said first PCR product; and performing a second polymerase chain reaction, thereby generating a second PCR product.

One aspect of the present invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185, or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of the preceding paragraph. In one embodiment, the cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-185.

Another aspect of the present invention is the method described four paragraphs above in which the second cDNA strand is made by contacting said first cDNA strand with a second primer comprising at least 15 consecutive nucleotides of the sequences of SEQ ID NOs: 38-185; hybridizing said second primer to said first strand cDNA; and extending said hybridized second primer to generate said second cDNA strand.

Another aspect of the present invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein partially encoded by one of SEQ ID NOs 38-185 or comprising a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method described in the preceding paragraph. In one embodiment, the cDNA comprises the full protein coding sequence partially included in of one of the sequences of SEQ ID NOs: 38-185.

Another aspect of the present invention is a method of making a protein comprising one of the sequences of SEQ ID NOs: 186-333, comprising the steps of obtaining a cDNA encoding the full protein sequence partially included in one of the sequences of sequence of SEQ ID NOs: 38-185; inserting said cDNA in an expression vector such that said cDNA is

10

15

20

25

operably linked to a promoter; introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA; and isolating said protein.

Another aspect of the present invention is an isolated protein obtainable by the method described in the preceding paragraph.

Another aspect of the present invention is a method of obtaining a promoter DNA comprising the steps of obtaining DNAs located upstream of the nucleic acids of SEQ ID NOs: 38-185 or the sequences complementary thereto; screening said upstream DNAs to identify a promoter capable of directing transcription initiation; and isolating said DNA comprising said identified promoter. In one embodiment, the obtaining step comprises chromosome walking from said nucleic acids of SEQ ID NOs: 38-185 or sequences complementary thereto. In another embodiment, the screening step comprises inserting said upstream sequences into a promoter reporter vector. In another embodiment, the screening step comprises identifying motifs in said upstream DNAs which are transcription factor binding sites or transcription start sites.

Another aspect of the present invention is an isolated promoter obtainable by the method described above.

Another aspect of the present invention is an isolated or purified protein comprising one of the sequences of SEQ ID NOs: 186-333.

Another aspect of the present invention is the inclusion of at least one of the sequences of SEQ ID NOs: 38-185, or one of the sequences complementary to the sequences of SEQ ID NOs: 38-185, or a fragment thereof of at least 15 consecutive nucleotides in an array of discrete ESTs or fragments thereof of at least 15 nucleotides in length. In one embodiment, the array includes at least two of the sequences of SEQ ID NOs: 38-185, the sequences complementary to the sequences of SEQ ID NOs: 38-185, or fragments thereof of at least 15 consecutive nucleotides. In another embodiment, the array includes at least five of the sequences of SEQ ID NOs: 38-185, the sequences complementary to the sequences of SEQ ID NOs: 38-185, or fragments thereof of at least 15 consecutive nucleotides.

Another aspect of the present invention is a promoter having a sequence selected from the group consisting of SEQ ID NOs: 31, 34, and 37.

10

15

20

30

# **Brief Description of the Drawings**

Figure 1 is a summary of a procedure for obtaining cDNAs which have been selected to include the 5' ends of the mRNAs from which they derived.

Figure 2 shows the distribution of Von Heijne scores for 5' ESTs in each of the categories described herein and the probability that these 5' ESTs encode a signal peptide.

Figure 3 summarizes a general method used to clone and sequence extended cDNAs containing sequences adjacent to 5' ESTs.

Figure 4 (description of promoters structure isolated from SignalTag 5' ESTs) provides a schematic description of promoters isolated and the way they are assembled with the corresponding 5' tags.

# **Detailed Description of the Preferred Embodiment**

Table IV is an analysis of the 43 amino acids located at the N terminus of all human SwissProt proteins to determine the frequency of false positives and false negatives using the techniques for signal peptide identification described herein.

Table V shows the distribution of 5' ESTs in each category described herein and the number of 5' ESTs in each category having a given minimum Von Heijne's score.

Table VI shows the distribution of 5' ESTs in each category described herein with respect to the tissue from which the 5' ESTs of the corresponding mRNA were obtained.

Table VII describes the transcription factor binding sites present in each of these promoters.

# I. General Methods for Obtaining 5' ESTs derived from mRNAs with intact 5' ends

In order to obtain the 5' ESTs of the present invention, mRNAs with intact 5' ends must be obtained. Currently, there are two approaches for obtaining such mRNAs with intact 5' ends as described below: either chemical (1) or enzymatic (2).

# 1. Chemical Methods for Obtaining mRNAs having Intact 5' Ends

One of these approaches is a chemical modification method involving derivatization of the 5' ends of the mRNAs and selection of the derivatized mRNAs. The 5' ends of eukaryotic mRNAs possess a structure referred to as a "cap" which comprises a guanosine

10

15

methylated at the 7 position. The cap is joined to the first transcribed base of the mRNA by a 5', 5'-triphosphate bond. In some instances, the 5' guanosine is methylated in both the 2 and 7 positions. Rarely, the 5' guanosine is trimethylated at the 2, 7 and 7 positions. In the chemical method for obtaining mRNAs having intact 5' ends, the 5' cap is specifically derivatized and coupled to a reactive group on an immobilizing substrate. This specific derivatization is based on the fact that only the ribose linked to the methylated guanosine at the 5' end of the mRNA and the ribose linked to the base at the 3' terminus of the mRNA, possess 2', 3'-cis diols.

Optionally, the 2', 3'-cis diol of the 3' terminal ribose may be chemically modified, substituted, converted, or eliminated, leaving only the ribose linked to the methylated guanosine at the 5' end of the mRNA with a 2', 3'-cis diol. A variety of techniques are available for eliminating the 2', 3'-cis diol on the 3' terminal ribose. For example, controlled alkaline hydrolysis may be used to generate mRNA fragments in which the 3' terminal ribose is a 3'-phosphate, 2'-phosphate or (2', 3')-cyclophosphate. Thereafter, the fragment which includes the original 3' ribose may be eliminated from the mixture through chromatography on an oligodT column. Alternatively, a base which lacks the 2', 3'-cis diol may be added to the 3' end of the mRNA using an RNA ligase such as T4 RNA ligase. Example 1 below describes a method for ligation of a nucleoside diphosphate to the 3' end of messenger RNA.

20

25

30

## **EXAMPLE 1**

# Ligation of the Nucleoside Diphosphate pCp to the 3' End of mRNA.

One µg of RNA was incubated in a final reaction medium of 10 µl in the presence of 5 U of T<sub>4</sub> phage RNA ligase in the buffer provided by the manufacturer (Gibco - BRL), 40 U of the RNase inhibitor RNasin (Promega) and, 2 µl of <sup>32</sup>pCp (Amersham #PB 10208). The incubation was performed at 37°C for 2 hours or overnight at 7-8°C.

Following modification or elimination of the 2', 3'-cis diol at the 3' ribose, the 2', 3'-cis diol present at the 5' end of the mRNA may be oxidized using reagents such as NaBH<sub>1</sub>, NaBH<sub>2</sub>CN, or sodium periodate, thereby converting the 2', 3'-cis diol to a dialdehyde.

10

15

Example 2 describes the oxidation of the 2', 3'-cis diol at the 5' end of the mRNA with sodium periodate.

#### **EXAMPLE 2**

# Oxidation of 2', 3'-cis diol at the 5' End of the mRNA with Sodium Periodate

0.1 OD unit of either a capped oligoribonucleotide of 47 nucleotides (including the cap) or an uncapped oligoribonucleotide of 46 nucleotides were treated as follows. The oligoribonucleotides were produced by *in vitro* transcription using the transcription kit "AmpliScribe T7" (Epicentre Technologies). As indicated below, the DNA template for the RNA transcript contained a single cytosine. To synthesize the uncapped RNA, all four NTPs were included in the *in vitro* transcription reaction. To obtain the capped RNA, GTP was replaced by an analogue of the cap, m7G(5')ppp(5')G. This compound, recognized by the polymerase, was incorporated into the 5' end of the nascent transcript during the initiation of transcription but was not incorporated during the extension step. Consequently, the resulting RNA contained a cap at its 5' end. The sequences of the oligoribonucleotides produced by the *in vitro* transcription reaction were:

+Cap:

5'm7GpppGCAUCCUACUCCCAUCCAAUUCCACCCUAACUCCUCCCAUCUCCAC3' (SEQ ID NO:1)

20 \_ -Cap:

25

30

5'-pppGCAUCCUACUCCAUCCAAUUCCACCCUAACUCCUCCCAUCUCCAC-3' (SEQ ID NO:2)

The oligoribonucleotides were dissolved in 9 µl of acetate buffer (0.1 M sodium acetate, pH 5.2) and 3 µl of freshly prepared 0.1 M sodium periodate solution. The mixture was incubated for 1 hour in the dark at 4°C or room temperature. Thereafter, the reaction was stopped by adding 4 µl of 10% ethylene glycol. The product was ethanol precipitated, resuspended in at least 10 µl of water or appropriate buffer and dialyzed against water.

The resulting aldehyde groups may then be coupled to molecules having a reactive amine group, such as hydrazine, carbazide, thiocarbazide or semicarbazide groups, in order to facilitate enrichment of the 5' ends of the mRNAs. Molecules having reactive amine groups

which are suitable for use in selecting mRNAs having intact 5' ends include avidin, proteins, antibodies, vitamins, ligands capable of specifically binding to receptor molecules, or oligonucleotides. Example 3 below describes the coupling of the resulting dialdehyde to biotin.

5

10

#### **EXAMPLE 3**

## Coupling of the Dialdehyde at the 5' End of Transcripts with Biotin

The oxidation product obtained in Example 2 was dissolved in 50  $\mu$ l of sodium acetate at a pH between 5 and 5.2 and 50  $\mu$ l of freshly prepared 0.02 M solution of biotin hydrazide in a methoxyethanol/water mixture (1:1) of formula:

In the compound used in these experiments, n=5. However, it will be appreciated that other commercially available hydrazides may also be used, such as molecules of the above formula in which n varies from 0 to 5. The mixture was then incubated for 2 hours at 37°C, precipitated with ethanol and dialyzed against distilled water. Example 4 demonstrates the specificity of the biotinylation reaction.

#### **EXAMPLE 4**

20

25

15

# Specificity of Biotinylation of Capped Transcripts

The specificity of the biotinylation for capped mRNAs was evaluated by gel electrophoresis of the following samples:

Sample 1. The 46 nucleotide uncapped *in vitro* transcript prepared as in Example 2 and labeled with <sup>32</sup>pCp as described in Example 1.

Sample 2. The 46 nucleotide uncapped *in vitro* transcript prepared as in Example 2, labeled with <sup>32</sup>pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.

Sample 3. The 47 nucleotide capped *in vitro* transcript prepared as in Example 2 and labeled with <sup>32</sup>pCp as described in Example 1.

Sample 4. The 47 nucleotide capped *in vitro* transcript prepared as in Example 2, labeled with <sup>32</sup>pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.

Samples 1 and 2 had identical migration rates, demonstrating that the uncapped RNAs were not oxidized and biotinylated. Sample 3 migrated more slowly than Samples 1 and 2, while Sample 4 exhibited the slowest migration. The difference in migration of the RNAs in Samples 3 and 4 demonstrates that the capped RNAs were specifically biotinylated.

10

5

In some cases, mRNAs having intact 5' ends may be enriched by binding the molecule containing a reactive amine group to a suitable solid phase substrate such as the inside of the vessel containing the mRNAs, magnetic beads, chromatography matrices, or nylon or nitrocellulose membranes. For example, where the molecule having a reactive amine group is biotin, the solid phase substrate may be coupled to avidin or streptavidin. Alternatively, where the molecule having the reactive amine group is an antibody or receptor ligand, the solid phase substrate may be coupled to the cognate antigen or receptor. Finally, where the molecule having a reactive amine group comprises an oligonucleotide, the solid phase substrate may comprise a complementary oligonucleotide.

20

25

15

The mRNAs having intact 5' ends may be released from the solid phase following the enrichment procedure. For example, where the dialdehyde is coupled to biotin hydrazide and the solid phase comprises streptavidin, the mRNAs may be released from the solid phase by simply heating to 95 degrees Celsius in 2% SDS. In some methods, the molecule having a reactive amine group may also be cleaved from the mRNAs having intact 5' ends following enrichment. Example 5 describes the capture of biotinylated mRNAs with streptavidin coated beads and the release of the biotinylated mRNAs from the beads following enrichment.

#### **EXAMPLE 5**

## Capture and Release of Biotinylated mRNAs Using Streptavidin Coated Beads

The streptavidin coated magnetic beads were prepared according to the manufacturer's instructions (CPG Inc., USA). The biotinylated mRNAs were added to a

15

20

hybridization buffer (1.5 M NaCl, pH 5 - 6). After incubating for 30 minutes, the unbound and nonbiotinylated material was removed. The beads were then washed several times in water with 1% SDS. The beads thus obtained were incubated for 15 minutes at 95°C in water containing 2% SDS.

Example 6 demonstrates the efficiency with which biotinylated mRNAs were recovered from the streptavidin coated beads.

#### **EXAMPLE 6**

## Efficiency of Recovery of Biotinylated mRNAs

The efficiency of the recovery procedure was evaluated as follows. Capped RNAs were labeled with <sup>32</sup>pCp, oxidized, biotinylated and bound to streptavidin coated beads as described above. Subsequently, the bound RNAs were incubated for 5, 15 or 30 minutes at 95°C in the presence of 2% SDS.

The products of the reaction were analyzed by electrophoresis on 12% polyacrylamide gels under denaturing conditions (7 M urea). The gels were subjected to autoradiography. During this manipulation, the hydrazone bonds were not reduced.

Increasing amounts of nucleic acids were recovered as incubation times in 2% SDS increased, demonstrating that biotinylated mRNAs were efficiently recovered.

In an alternative method for obtaining mRNAs having intact 5' ends, an oligonucleotide which has been derivatized to contain a reactive amine group is specifically coupled to mRNAs having an intact cap. Preferably, the 3' end of the mRNA is blocked prior to the step in which the aldehyde groups are joined to the derivatized oligonucleotide, as described above, so as to prevent the derivatized oligonucleotide from being joined to the 3' end of the mRNA using T4 RNA ligase as described in example 1. However, as discussed above, blocking the 3' end of the mRNA is an optional step. Derivatized oligonucleotides may be prepared as described in Example 7.

#### **EXAMPLE 7**

## **Derivatization of Oligonucleotides**

An oligonucleotide phosphorylated at its 3' end was converted to a 3' hydrazide in 3' by treatment with an aqueous solution of hydrazine or of dihydrazide of the formula  $H_2N(R1)NH_2$  at about 1 to 3 M, and at pH 4.5 at a temperature of 8°C overnight. This incubation was performed in the presence of a carbodiimide type agent soluble in water such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide at a final concentration of 0.3 M.

The derivatized oligonucleotide was then separated from the other agents and products using a standard technique for isolating oligonucleotides.

As discussed above, the mRNAs to be enriched may be treated to eliminate the 3' OH groups which may be present thereon. This may be accomplished by enzymatic ligation of sequences lacking a 3' OH, such as pCp, as described in Example 1. Alternatively, the 3' OH groups may be eliminated by alkaline hydrolysis as described in Example 8 below.

## 15

20

10

5

#### **EXAMPLE 8**

#### Elimination of 3' OH Groups of mRNA Using Alkaline Hydrolysis

In a total volume of 100  $\mu$ l of 0.1 N sodium hydroxide, 1.5  $\mu$ g mRNA is incubated for 40 to 60 minutes at 4°C. The solution is neutralized with acetic acid and precipitated with ethanol.

Following the optional elimination of the 3' OH groups, the diol groups at the 5' ends of the mRNAs are oxidized as described below in Example 9.

#### **EXAMPLE 9**

## Oxidation of Diols of mRNA

Up to 1 OD unit of RNA was dissolved in 9 μl of buffer (0.1 M sodium acetate, pH 6-7) or water and 3 μl of freshly prepared 0.1 M sodium periodate solution. The reaction was incubated for 1 h in the dark at 4°C or room temperature. Following the incubation, the reaction was stopped by adding 4 μl of 10% ethylene glycol. Thereafter the mixture was incubated at room temperature for 15 minutes. After ethanol precipitation, the product was resuspended in at least 10 μl of water or appropriate buffer and dialyzed against water.

10

15

20

25

30

Following oxidation of the diol groups at the 5' ends of the mRNAs, the derivatized oligonucleotide was joined to the resulting aldehydes as described in Example 10.

#### **EXAMPLE 10**

# Ligature of Aldehydes of mRNA to Derivatized Oligonucleotides

The oxidized mRNA was dissolved in an acidic medium such as 50 µl of sodium acetate pH 4-6. Fifty µl of a solution of the derivatized oligonucleotide were added in order to obtain an mRNA: derivatized oligonucleotide ratio of 1:20. The mixture was reduced with a borohydride and incubated for 2 h at 37°C or overnight (14 h) at 10°C. The mixture was then ethanol precipitated, resuspended in 10 µl or more of water or appropriate buffer and dialyzed against distilled water. If desired, the resulting product may be analyzed using acrylamide gel electrophoresis, HPLC analysis, or other conventional techniques.

Following the attachment of the derivatized oligonucleotide to the mRNAs, a reverse transcription reaction may be performed as described in Example 11 below.

#### **EXAMPLE 11**

# Reverse Transcription of mRNAs Ligatured to Derivatized Oligonucleotides

An oligodeoxyribonucleotide was derivatized as follows. Three OD units of an oligodeoxyribonucleotide of sequence 5'ATCAAGAATTCGCACGAGACCATTA3' (SEQ ID NO:3) having 5'-OH and 3'-P ends were dissolved in 70 µl of a 1.5 M hydroxybenzotriazole solution, pH 5.3, prepared in dimethylformamide/water (75:25) containing 2 µg of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide. The mixture was incubated for 2 h 30 min at 22°C and then precipitated twice in LiClO<sub>4</sub>/acetone. The pellet was resuspended in 200 µl of 0.25 M hydrazine and incubated at 8°C from 3 to 14 h. Following the hydrazine reaction, the mixture was precipitated twice in LiClO<sub>4</sub>/acetone.

The messenger RNAs to be reverse transcribed were extracted from blocks of placenta having sides of 2 cm which had been stored at -80°C. The total RNA was extracted using conventional acidic phenol techniques. Oligo-dT chromatography was used to purify the mRNAs. The integrity of the mRNAs was checked by Northern-blotting.

10

15

20

25

30

The diol groups on 7 µg of the placental mRNAs were oxidized as described above in Example 9. The derivatized oligonucleotide was joined to the mRNAs as described in Example 10 above except that the precipitation step was replaced by an exclusion chromatography step to remove derivatized oligodeoxyribonucleotides which were not joined to mRNAs. Exclusion chromatography was performed as follows:

Ten ml of Ultrogel AcA34 (BioSepra#230151) gel, a mix of agarose and acrylamide, were equilibrated in 50 ml of a solution of 10 mM Tris pH 8.0, 300 mM NaCl, 1 mM EDTA, and 0.05% SDS. The mixture was allowed to sediment. The supernatant was eliminated and the gel was resuspended in 50 ml of buffer. This procedure was repeated 2 or 3 times.

A glass bead (diameter 3 mm) was introduced into a 2 ml disposable pipette (length 25 cm). The pipette was filled with the gel suspension until the height of the gel stabilized at 1 cm from the top of the pipette. The column was then equilibrated with 20 ml of equilibration buffer (10 mM Tris HCl pH 7.4, 20 mM NaCl).

Ten  $\mu$ l of the mRNA which had reacted with the derivatized oligonucleotide were mixed in 39  $\mu$ l of 10 mM urea and 2  $\mu$ l of blue-glycerol buffer, which had been prepared by dissolving 5 mg of bromophenol blue in 60% glycerol (v/v), and passing the mixture through a 0.45  $\mu$ m diameter filter.

The column was then loaded with the mRNAs coupled to the oligonucleotide. As soon as the sample had penetrated, equilibration buffer was added. Hundred µl fractions were then collected. Derivatized oligonucleotide which had not been attached to mRNA appeared in fraction 16 and later fractions. Thus, fractions 3 to 15 were combined and precipitated with ethanol.

To determine whether the derivatized oligonucleotide was actually linked to mRNA, one tenth of the combined fractions were spotted twice on a nylon membrane and hybridized to a radioactive probe using conventional techniques. The <sup>32</sup>P labeled probe used in these hybridizations was an oligodeoxyribonucleotide of sequence 5'TAATGGTCTCGTGCGAATTCTTGAT3' (SEQ ID NO:4) anticomplementary to the derivatized oligonucleotide. A signal observed after autoradiography, indicated that the derivatized oligonucleotide had been truly joined to the mRNA.

The remaining nine tenth of the mRNAs which had reacted with the derivatized oligonucleotide was reverse transcribed as follows. A reverse transcription reaction was

10

15

20

carried out with reverse transcriptase following the manufacturer's instructions and 50 pmol of nonamers with random sequence as primers.

To ensure that reverse transcription had been carried out through the cap structure, two types of experiments were performed.

In the first approach, after elimination of RNA of the cDNA:RNA heteroduplexes obtained from the reverse transcription reaction by an alkaline hydrolysis, a portion of the resulting single stranded cDNAs was spotted on a positively charged membrane and hybridized, using conventional methods, to a <sup>32</sup>P labeled probe having a sequence identical to that of the derivatized oligonucleotide. Control spots containing, 1 pmol, 100 finol, 50 finol, 10 finol and 1 finol of a control oligodeoxyribonucleotide of sequence identical to that of the derivatized oligonucleotide were included. The signal observed in the spots containing the cDNA indicated that approximately 15 finol of the derivatized oligonucleotide had been reverse transcribed. These results demonstrate that the reverse transcription can be performed through the cap and, in particular, that reverse transcriptase crosses the 5'-P-P-P-5' bond of the cap of eukaryotic messenger RNAs.

In the second type of experiment, the single stranded cDNAs obtained from the above first strand synthesis were used as template for PCR reactions. Two types of reactions were carried out. First, specific amplification of the mRNAs for alpha globin, dehydrogenase, pp15 and elongation factor E4 were carried out using the following pairs of oligodeoxyribonucleotide primers.

#### alpha-globin

GLO-S: 5'CCG ACA AGA CCA ACG TCA AGG CCG C3' (SEQ ID NO:5)
GLO-As: 5'TCA CCA GCA GGC AGT GGC TTA GGA G 3' (SEQ ID NO:6)

25

#### dehydrogenase

3 DH-S: 5'AGT GAT TCC TGC TAC TTT GGA TGG C3' (SEQ ID NO:7)
3 DH-As: 5'GCT TGG TCT TGT TCT GGA GTT TAG A3' (SEQ ID NO:8)

30

pp15

PP15-S: 5'TCC AGA ATG GGA GAC AAG CCA ATT T3' (SEQ ID NO:9)

# PP15-As: 5'AGG GAG GAG GAA ACA GCG TGA GTC C3' (SEQ ID NO:10)

## Elongation factor E4

EFA1-S: 5'ATG GGA AAG GAA AAG ACT CAT ATC A3' (SEQ ID NO:11)

5 EF1A-As: 5'AGC AGC AAC AAT CAG GAC AGC ACA G3' (SEQ ID NO:12)

Second, non specific amplifications were also carried out with the antisense oligodeoxyribonucleotides of the pairs described above and with a primer derived from the sequence of the derivatized oligodeoxyribonucleotide (5'ATCAAGAATTCGCACGAGACCATTA3') (SEQ ID NO:13).

One twentieth of the following RT-PCR product samples were run on a 1.5% agarose gel and stained with ethidium bromide.

- Sample 1: The products of a PCR reaction using the globin primers of SEQ ID NOs 5 and 6 in the presence of cDNA.
- Sample 2: The products of a PCR reaction using the globin primers of SEQ ID NOs 5 and 6 in the absence of added cDNA.
  - Sample 3: The products of a PCR reaction using the dehydrogenase primers of SEQ ID NOs 7 and 8 in the presence of cDNA.
- Sample 4: The products of a PCR reaction using the dehydrogenase primers of SEQ 20 ID NOs 7 and 8 in the absence of added cDNA.
  - Sample 5: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the presence of cDNA.
  - Sample 6: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the absence of added cDNA.
- Sample 7: The products of a PCR reaction using the EIF4 primers of SEQ ID NOs 11 and 12 in the presence of added cDNA.
  - Sample 8: The products of a PCR reaction using the EIF4 primers of SEQ ID NOs 11 and 12 in the absence of added cDNA.
- A band of the size expected for the PCR product was observed only in samples 1, 3, 30 5 and 7, thus indicating the presence of the corresponding sequence in the cDNA population.

10

15

20

PCR reactions were also carried out with the antisense oligonucleotides of the globin and dehydrogenase primers (SEQ ID NOs 6 and 8) and an oligonucleotide whose sequence corresponds to that of the derivatized oligonucleotide. The presence of PCR products of the expected size in the samples equivalent to above samples 1 and 3 indicated that the derivatized oligonucleotide had been linked to mRNA.

The above examples summarize the chemical procedure for enriching mRNAs for those having intact 5' ends as illustrated in Figure 1. Further detail regarding the chemical approaches for obtaining such mRNAs are disclosed in International Application No. WO96/34981, published November 7, 1996, which is incorporated herein by reference. Strategies based on the above chemical modifications to the 5' cap structure may be utilized to generate cDNAs selected to include the 5' ends of the mRNAs from which they derived. In one version of such procedures, the 5' ends of the mRNAs are modified as described Thereafter, a reverse transcription reaction is conducted to extend a primer complementary to the 5' end of the mRNA. Single stranded RNAs are eliminated to obtain a population of cDNA/mRNA heteroduplexes in which the mRNA includes an intact 5' end. The resulting heteroduplexes may be captured on a solid phase coated with a molecule capable of interacting with the molecule used to derivatize the 5' end of the mRNA. Thereafter, the strands of the heteroduplexes are separated to recover single stranded first cDNA strands which include the 5' end of the mRNA. Second strand cDNA synthesis may then proceed using conventional techniques. For example, the procedures disclosed in WO 96/34981 or in Carninci. et al., Genomics 37:327-336, 1996, the disclosures of which are incorporated herein by reference, may be employed to select cDNAs which include the sequence derived from the 5' end of the coding sequence of the mRNA.

Following ligation of the oligonucleotide tag to the 5' cap of the mRNA, a reverse transcription reaction is conducted to extend a primer complementary to the mRNA to the 5' end of the mRNA. Following elimination of the RNA component of the resulting heteroduplex using standard techniques, second strand cDNA synthesis is conducted with a primer complementary to the oligonucleotide tag.

5.

10

15

20

25

30

## 2. Enzymatic Methods for Obtaining mRNAs having Intact 5' Ends

Other techniques for selecting cDNAs extending to the 5' end of the mRNA from which they are derived are fully enzymatic. Some versions of these techniques are disclosed in Dumas Milne Edwards J.B. (Doctoral Thesis of Paris VI University, Le clonage des ADNc complets: difficultes et perspectives nouvelles. Apports pour l'etude de la regulation de l'expression de la tryptophane hydroxylase de rat, 20 Dec. 1993), EPO 625572 and Kato et al., Gene 150:243-250, 1994, the disclosures of which are incorporated herein by reference.

Briefly, in such approaches, isolated mRNA is treated with alkaline phosphatase to remove the phosphate groups present on the 5' ends of uncapped incomplete mRNAs. Following this procedure, the cap present on full length mRNAs is enzymatically removed with a decapping enzyme such as T4 polynucleotide kinase or tobacco acid pyrophosphatase. An oligonucleotide, which may be either a DNA oligonucleotide or a DNA-RNA hybrid oligonucleotide having RNA at its 3' end, is then ligated to the phosphate present at the 5' end of the decapped mRNA using T4 RNA ligase. The oligonucleotide may include a restriction site to facilitate cloning of the cDNAs following their synthesis. Example 12 below describes one enzymatic method based on the doctoral thesis of Dumas.

#### **EXAMPLE 12**

#### Enzymatic Approach for Obtaining 5' ESTs

Twenty micrograms of PolyA+ RNA were dephosphorylated using Calf Intestinal Phosphatase (Biolabs). After a phenol chloroform extraction, the cap structure of mRNA was hydrolysed using the Tobacco Acid Pyrophosphatase (purified as described by Shinshi et al.., Biochemistry 15: 2185-2190, 1976) and a hemi 5'DNA/RNA-3' oligonucleotide having an unphosphorylated 5' end, a stretch of adenosine ribophosphate at the 3' end, and an EcoRI site near the 5' end was ligated to the 5'P ends of mRNA using the T4 RNA ligase (Biolabs). Oligonucleotides suitable for use in this procedure are preferably 30 to 50 bases in length. Oligonucleotides having an unphosphorylated 5' end may be synthesized by adding a fluorochrome at the 5' end. The inclusion of a stretch of adenosine ribophosphates at the 3' end of the oligonucleotide increases ligation efficiency. It will be appreciated that the oligonucleotide may contain cloning sites other than EcoRI.

Following ligation of the oligonucleotide to the phosphate present at the 5' end of the decapped mRNA, first and second strand cDNA synthesis is carried out using conventional methods or those specified in EP0 625,572 and Kato et al. supra, and Dumas Milne Edwards, supra, the disclosures of which are incorporated herein by reference. The resulting cDNA may then be ligated into vectors such as those disclosed in Kato et al., supra or other nucleic acid vectors known to those skilled in the art using techniques such as those described in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989, the disclosure of which is incorporated herein by reference.

10

5

## II. Obtention and Characterization of the 5' ESTs of the Present Invention

The 5' ESTs of the present invention were obtained using the aforementioned chemical and enzymatic approaches for enriching mRNAs for those having intact 5' ends as decribed below.

15

## 1. Obtention of 5' ESTS Using mRNAs with Intact 5' Ends

First, mRNAs were prepared as described in Example 13 below.

#### **EXAMPLE 13**

20

25

30

## Preparation of mRNA With Intact 5' Ends

Total human RNAs or polyA<sup>+</sup> RNAs derived from 29 different tissues were respectively purchased from LABIMO and CLONTECH and used to generate 44 cDNA libraries as follows. The purchased RNA had been isolated from cells or tissues using acid guanidium thiocyanate-phenol-chloroform extraction (Chomczyniski and Sacchi, *Analytical Biochemistry* 162:156-159, 1987). PolyA<sup>+</sup> RNA was isolated from total RNA (LABIMO) by two passes of oligo dT chromatography, as described by Aviv and Leder, *Proc. Natl. Acad. Sci. USA* 69:1408-1412, 1972 in order to eliminate ribosomal RNA.

The quality and the integrity of the polyA+ RNAs were checked. Northern blots hybridized with a globin probe were used to confirm that the mRNAs were not degraded. Contamination of the polyA+ mRNAs by ribosomal sequences was checked using Northern blots and a probe derived from the sequence of the 28S rRNA. Preparations of mRNAs with

10

15

less than 5% of rRNAs were used in library construction. To avoid constructing libraries with RNAs contaminated by exogenous sequences (prokaryotic or fungal), the presence of bacterial 16S ribosomal sequences or of two highly expressed fungal mRNAs was examined using PCR.

Following preparation of the mRNAs, the above described chemical and/or the enzymatic procedures for enriching mRNAs for thoses having intact 5' ends were employed to obtain 5' ESTs from various tissues. In both approaches, an oligonucleotide tag was attached to the 5' ends of the mRNAs. The oligonucleotide tag had an EcoRI site therein to facilitate later cloning procedures. To facilitate the processing of single stranded and double stranded cDNA obtained in the construction of the librairies, the same nucleotidic sequence was used to design the ligated oligonucleotide in both chemical and enzymatic approaches. Nevertheless, in the chemical procedure, the tag used was an oligodeoxyribonucleotide which was linked to the cap of the mRNA whereas in the enzymatic ligation, the tag was a chimeric hemi 5'DNA/RNA3' oligonucleotide which was ligated to the 5' end of decapped mRNA as described in example 12.

Following attachment of the oligonucleotide tag to the mRNA by either the chemical or enzymatic methods, the integrity of the mRNA was examined by performing a Northern blot with 200 to 500 ng of mRNA using a probe complementary to the oligonucleotide tag before performing the first strand synthesis as described in example 14.

20

25

30

#### **EXAMPLE 14**

## cDNA Synthesis Using mRNA Templates Having Intact 5' Ends

For the mRNAs joined to oligonucleotide tags using both the chemical and enzymatic methods, first strand cDNA synthesis was performed using the Superscript II (Gibco BRL) or the Rnase H Minus M-MLV (Promega) reverse transcriptase with random nonamers as primers. In order to protect internal EcoRI sites in the cDNA from digestion at later steps in the procedure, methylated dCTP was used for first strand synthesis. After removal of RNA by an alkaline hydrolysis, the first strand of cDNA was precipitated using isopropanol in order to eliminate residual primers.

For both the chemical and the enzymatic methods, the second strand of the cDNA was synthesized with a Klenow fragment using a primer corresponding to the 5' end of the

10

15

ligated oligonucleotide described in Example 12. Preferably, the primer is 20-25 bases in length. Methylated dCTP was also used for second strand synthesis in order to protect internal EcoRI sites in the cDNA from digestion during the cloning process.

Following cDNA synthesis, the cDNAs were cloned into pBlueScript as described in Example 15 below.

#### **EXAMPLE 15**

# Cloning of cDNAsderived from mRNA with intact 5' ends into BlueScript

Following second strand synthesis, the ends of the cDNA were blunted with T4 DNA polymerase (Biolabs) and the cDNA was digested with EcoRI. Since methylated dCTP was used during cDNA synthesis, the EcoRI site present in the tag was the only hemi-methylated site, hence the only site susceptible to EcoRI digestion. The cDNA was then size fractionated using exclusion chromatography (AcA, Biosepra) and fractions corresponding to cDNAs of more than 150 bp were pooled and ethanol precipitated. The cDNA was directionally cloned into the SmaI and EcoRI ends of the phagemid pBlueScript vector (Stratagene). The ligation mixture was electroporated into bacteria and propagated under appropriate antibiotic selection.

Clones containing the oligonucleotide tag attached were then selected as described in Example 16 below.

20

25

30

#### **EXAMPLE 16**

# Selection of Clones Having the Oligonucleotide Tag Attached Thereto

The plasmid DNAs containing 5' EST libraries made as described above were purified (Qiagen). A positive selection of the tagged clones was performed as follows. Briefly, in this selection procedure, the plasmid DNA was converted to single stranded DNA using gene II endonuclease of the phage F1 in combination with an exonuclease (Chang et al., Gene 127:95-8, 1993) such as exonuclease III or T7 gene 6 exonuclease. The resulting single stranded DNA was then purified using paramagnetic beads as described by Fry et al., Biotechniques, 13: 124-131, 1992. In this procedure, the single stranded DNA was hybridized with a biotinylated oligonucleotide having a sequence corresponding to the 3' end of the oligonucleotide described in Example 13. Preferably, the primer has a length of 20-25

bases. Clones including a sequence complementary to the biotinylated oligonucleotide were captured by incubation with streptavidin coated magnetic beads followed by magnetic selection. After capture of the positive clones, the plasmid DNA was released from the magnetic beads and converted into double stranded DNA using a DNA polymerase such as the ThermoSequenase obtained from Amersham Pharmacia Biotech. Alternatively, protocoles such as the one described in the Gene Trapper kit available from Gibco BRL may be used. The double stranded DNA was then electroporated into bacteria. The percentage of positive clones having the 5' tag oligonucleotide was estimated to typically rank between 90 and 98% using dot blot analysis.

Following electroporation, the libraries were ordered in 384-microtiter plates (MTP). A copy of the MTP was stored for future needs. Then the libraries were transferred into 96 MTP and sequenced as described below.

### **EXAMPLE 17**

15

20

25

30

10

5

## Sequencing of Inserts in Selected Clones

Plasmid inserts were first amplified by PCR on PE 9600 thermocyclers (Perkin-Elmer, Applied Biosystems Division, Foster City, CA), using standard SETA-A and SETA-B primers (Genset SA), AmpliTaqGold (Perkin-Elmer), dNTPs (Boehringer), buffer and cycling conditions as recommended by the Perkin-Elmer Corporation.

PCR products were then sequenced using automatic ABI Prism 377 sequencers (Perkin Elmer). Sequencing reactions were performed using PE 9600 thermocyclers with standard dye-primer chemistry and ThermoSequenase (Amersham Pharmacia Biotech). The primers used were either T7 or 21M13 (available from Genset SA) as appropriate. The primers were labeled with the JOE, FAM, ROX and TAMRA dyes. The dNTPs and ddNTPs used in the sequencing reactions were purchased from Boehringer. Sequencing buffer, reagent concentrations and cycling conditions were as recommended by Amersham.

Following the sequencing reaction, the samples were precipitated with ethanol, resuspended in formamide loading buffer, and loaded on a standard 4% acrylamide gel. Electrophoresis was performed for 2.5 hours at 3000V on an ABI 377 sequencer, and the sequence data were collected and analyzed using the ABI Prism DNA Sequencing Analysis Software, version 2.1.2.

10

15

20

25

30

## 2. Computer analysis of the Obtained 5' ESTs: Construction of NetGene and SignalTag databases

The sequence data from the 44 cDNA libraries made as described above were transferred to a proprietary database, where quality control and validation steps were performed. A proprietary base-caller, working using a Unix system, automatically flagged suspect peaks, taking into account the shape of the peaks, the inter-peak resolution, and the noise level. The proprietary base-caller also performed an automatic trimming. Any stretch of 25 or fewer bases having more than 4 suspect peaks was considered unreliable and was discarded. Sequences corresponding to cloning vector or ligation oligonucleotides were automatically removed from the EST sequences. However, the resulting EST sequences may contain 1 to 5 bases belonging to the above mentioned sequences at their 5' end. If needed, these can easily be removed on a case to case basis.

Following sequencing as described above, the sequences of the 5' ESTs were entered in NetGene™, a proprietary database called for storage and manipulation as described below. It will be appreciated by those skilled in the art that the data could be stored and manipulated on any medium which can be read and accessed by a computer. Computer readable media include magnetically, optically, or electronically readable media. For example, the computer readable media may be a hard disc, a floppy disc, a magnetic tape, CD-ROM, RAM, or ROM as well as other types of other media known to those skilled in the art.

In addition, the sequence data may be stored and manipulated in a variety of data processor programs in a diversity of formats. For instance, the sequence data may be stored as text in a word processing file, such as Microsoft WORD or WORDPERFECT or as an ASCII file in a variety of database programs familiar to those of skill in the art, such as DB2, SYBASE, or ORACLE.

The computer readable media on which the sequence information is stored may be in a personal computer, a network, a server or other computer systems known to those skilled in the art. The computer or other system preferably includes the storage media described above, and a processor for accessing and manipulating the sequence data. Once the sequence data has been stored, it may be manipulated and searched to locate those stored sequences which contain a desired nucleic acid sequence or which encode a protein having a particular functional domain. For example, the stored sequence information may be compared to other

10

15

known sequences to identify homologies, motifs implicated in biological function, or structural motifs.

Programs which may be used to search or compare the stored sequences include the MacPattern (EMBL), BLAST, and BLAST2 program series (NCBI), basic local alignment search tool programs for nucleotide (BLASTN) and peptide (BLASTX) comparisons (Altschul et al, J. Mol. Biol. 215: 403, 1990) and FASTA (Pearson and Lipman, Proc. Natl. Acad. Sci. USA 85: 2444, 1988). The BLAST programs then extend the alignments on the basis of defined match and mismatch criteria.

Motifs which may be detected using the above programs and those described in Example 28 include sequences encoding leucine zippers, helix-turn-helix motifs, glycosylation sites, ubiquitination sites, alpha helices, and beta sheets, signal sequences encoding signal peptides which direct the secretion of the encoded proteins, sequences implicated in transcription regulation such as homeoboxes, acidic stretches, enzymatic active sites, substrate binding sites, and enzymatic cleavage sites.

Before searching the cDNAs in the NetGene™ database for sequence motifs of interest, cDNAs derived from mRNAs which were not of interest were identified and eliminated from further consideration as described in Example 18 below.

### **EXAMPLE 18**

20

25

30

### Elimination of Undesired Sequences from Further Consideration

5' ESTs in the NetGene™ database which were derived from undesired sequences such as transfer RNAs, ribosomal RNAs, mitochondrial RNAs, prokaryotic RNAs, fungal RNAs, Alu sequences, L1 sequences, or repeat sequences were identified using the FASTA and BLASTN programs with the parameters listed in Table I.

To eliminate 5' ESTs encoding tRNAs from further consideration, the 5' EST sequences were compared to the sequences of 1190 known tRNAs obtained from EMBL release 38, of which 100 were human. The comparison was performed using FASTA on both strands of the 5' ESTs. Sequences having more than 80% homology over more than 60 nucleotides were identified as tRNA. Of the 144,341 sequences screened, 26 were identified as tRNAs and eliminated from further consideration.

10

15

20

25

30

To eliminate 5' ESTs encoding rRNAs from further consideration, the 5' EST sequences were compared to the sequences of 2497 known rRNAs obtained from EMBL release 38, of which 73 were human. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S=108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as rRNAs. Of the 144,341 sequences screened, 3,312 were identified as rRNAs and eliminated from further consideration.

To eliminate 5' ESTs encoding mtRNAs from further consideration, the 5' EST sequences were compared to the sequences of the two known mitochondrial genomes for which the entire genomic sequences are available and all sequences transcribed from these mitochondrial genomes including tRNAs, rRNAs, and mRNAs for a total of 38 sequences. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S=108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as mtRNAs. Of the 144,341 sequences screened, 6,110 were identified as mtRNAs and eliminated from further consideration.

Sequences which might have resulted from exogenous contaminants were eliminated from further consideration by comparing the 5' EST sequences to release 46 of the EMBL bacterial and fungal divisions using BLASTN with the parameter S=144. All sequences having more than 90% homology over at least 40 nucleotides were identified as exogenous contaminants. Of the 42 cDNA libraries examined, the average percentages of prokaryotic and fungal sequences contained therein were 0.2% and 0.5% respectively. Among these sequences, only one could be identified as a sequence specific to fungi. The others were either fungal or prokaryotic sequences having homologies with vertebrate sequences or including repeat sequences which had not been masked during the electronic comparison.

In addition, the 5' ESTs were compared to 6093 Alu sequences and 1115 L1 sequences to mask 5' ESTs containing such repeat sequences. 5' ESTs including THE and MER repeats, SSTR sequences or satellite, micro-satellite, or telomeric repeats were also eliminated from further consideration. On average, 11.5% of the sequences in the libraries contained repeat sequences. Of this 11.5%, 7% contained Alu repeats, 3.3% contained L1 repeats and the remaining 1.2% were derived from the other screened types of repetitive sequences. These percentages are consistent with those found in cDNA libraries prepared by

10

15

20

25

30

other groups. For example, the cDNA libraries of Adams et al. contained between 0% and 7.4% Alu repeats depending on the source of the RNA which was used to prepare the cDNA library (Adams et al., Nature 377:174, 1996).

The sequences of those 5' ESTs remaining after the elimination of undesirable sequences were compared with the sequences of known human mRNAs to determine the accuracy of the sequencing procedures described above.

#### **EXAMPLE 19**

## Measurement of Sequencing Accuracy by Comparison to Known Sequences

To further determine the accuracy of the sequencing procedure described above, the sequences of 5' ESTs derived from known sequences were identified and compared to the original known sequences. First, a FASTA analysis with overhangs shorter than 5 bp on both ends was conducted on the 5' ESTs to identify those matching an entry in the public human mRNA database. The 6655 5' ESTs which matched a known human mRNA were then realigned with their cognate mRNA and dynamic programming was used to include substitutions, insertions, and deletions in the list of "errors" which would be recognized. Errors occurring in the last 10 bases of the 5' EST sequences were ignored to avoid the inclusion of spurious cloning sites in the analysis of sequencing accuracy.

This analysis revealed that the sequences incorporated in the NetGene<sup>™</sup> database had an accuracy of more than 99.5%.

To determine the efficiency with which the above selection procedures select cDNAs which include the 5' ends of their corresponding mRNAs, the following analysis was performed.

#### **EXAMPLE 20**

### Determination of Efficiency of 5' EST Selection

To determine the efficiency at which the above selection procedures isolated 5' ESTs which included sequences close to the 5' end of the mRNAs from which they derived, the sequences of the ends of the 5' ESTs derived from the elongation factor 1 subunit α and

10

15

20

25

30

ferritin heavy chain genes were compared to the known cDNA sequences of these genes. Since the transcription start sites of both genes are well characterized, they may be used to determine the percentage of derived 5' ESTs which included the authentic transcription start sites.

For both genes, more than 95% of the obtained 5' ESTs actually included sequences close to or upstream of the 5' end of the corresponding mRNAs.

To extend the analysis of the reliability of the procedures for isolating 5' ESTs from ESTs in the NetGene™ database, a similar analysis was conducted using a database composed of human mRNA sequences extracted from GenBank database release 97 for comparison. The 5' ends of more than 85% of 5' ESTs derived from mRNAs included in the GeneBank database were located close to the 5' ends of the known sequence. As some of the mRNA sequences available in the GenBank database are deduced from genomic sequences, a 5' end matching with these sequences will be counted as an internal match. Thus, the method used here underestimates the yield of ESTs including the authentic 5' ends of their corresponding mRNAs.

The EST libraries made above included multiple 5' ESTs derived from the same mRNA. The sequences of such 5' ESTs were compared to one another and the longest 5' ESTs for each mRNA were identified. Overlapping cDNAs were assembled into continuous -sequences (contigs). The resulting continuous sequences were then compared to public databases to gauge their similarity to known sequences, as described in Example 21 below.

#### **EXAMPLE 21**

## Clustering of the 5' ESTs and Calculation of Novelty Indices for cDNA Libraries

For each sequenced EST library, the sequences were clustered by the 5' end. Each sequence in the library was compared to the others with BLASTN2 (direct strand, parameters S=107). ESTs with High Scoring Segment Pairs (HSPs) at least 25 bp long, having 95% identical bases and beginning closer than 10 bp from each EST 5' end were grouped. The longest sequence found in the cluster was used as representative of the group. A global clustering between libraries was then performed leading to the definition of super-contigs.

10

15

To assess the yield of new sequences within the EST libraries, a novelty rate (NR) was defined as: NR= 100 X (Number of new unique sequences found in the library/Total number of sequences from the library). Typically, novelty rating ranged between 10% and 41% depending on the tissue from which the EST library was obtained. For most of the libraries, the random sequencing of 5' EST libraries was pursued until the novelty rate reached 20%.

Following characterization as described above, the collection of 5' ESTs in NetGene<sup>TM</sup> was screened to identify those 5' ESTs bearing potential signal sequences as described in Example 22 below.

### **EXAMPLE 22**

### Identification of Potential Signal Sequences in 5' ESTs

The 5' ESTs in the NetGene<sup>TM</sup> database were screened to identify those having an uninterrupted open reading frame (ORF) longer than 45 nucleotides beginning with an ATG codon and extending to the end of the EST. Approximately half of the cDNA sequences in NetGene<sup>TM</sup> contained such an ORF. The ORFs of these 5' ESTs were then searched to identify potential signal motifs using slight modifications of the procedures disclosed in Von Heijne, Nucleic Acids Res. 14:4683-4690, 1986, the disclosure of which is incorporated 20 herein by reference. Those 5' EST sequences encoding a stretch of at least 15 amino acid long with a score of at least 3.5 in the Von Heijne signal peptide identification matrix were considered to possess a signal sequence. Those 5' ESTs which matched a known human mRNA or EST sequence and had a 5' end more than 20 nucleotides downstream of the known 5' end were excluded from further analysis. The remaining cDNAs having signal sequences therein were included in a database called SignalTag<sup>TM</sup>.

To confirm the accuracy of the above method for identifying signal sequences, the analysis of Example 23 was performed.

25

### **EXAMPLE 23**

## Confirmation of Accuracy of Identification of Potential Signal Sequences in 5' ESTs

The accuracy of the above procedure for identifying signal sequences encoding signal peptides was evaluated by applying the method to the 43 amino acids located at the N terminus of all human SwissProt proteins. The computed Von Heijne score for each protein was compared with the known characterization of the protein as being a secreted protein or a non-secreted protein. In this manner, the number of non-secreted proteins having a score higher than 3.5 (false positives) and the number of secreted proteins having a score lower than 3.5 (false negatives) could be calculated.

10

5

Using the results of the above analysis, the probability that a peptide encoded by the 5' region of the mRNA is in fact a genuine signal peptide based on its Von Heijne's score was calculated based on either the assumption that 10% of human proteins are secreted or the assumption that 20% of human proteins are secreted. The results of this analysis are shown in Figure 2 and in Table IV.

15

Using the above method of identification of secretory proteins, 5' ESTs of the following polypeptides known to be secreted were obtained: human glucagon, gamma interferon induced monokine precursor, secreted cyclophilin-like protein, human pleiotropin, and human biotinidase precursor. Thus, the above method successfully identified those 5' ESTs which encode a signal peptide.

20

25

30

To confirm that the signal peptide encoded by the 5' ESTs actually functions as a signal peptide, the signal sequences from the 5' ESTs may be cloned into a vector designed for the identification of signal peptides. Such vectors are designed to confer the ability to grow in selective medium only to host cells containing a vector with an operably linked signal sequence. For example, to confirm that a 5' EST encodes a genuine signal peptide, the signal sequence of the 5' EST may be inserted upstream and in frame with a non-secreted form of the yeast invertase gene in signal peptide selection vectors such as those described in U.S. Patent No. 5,536,637, the disclosure of which is incorporated herein by reference. Growth of host cells containing signal sequence selection vectors with the correctly inserted 5' EST signal sequence confirms that the 5' EST encodes a genuine signal peptide.

Alternatively, the presence of a signal peptide may be confirmed by cloning the extended cDNAs obtained using the ESTs into expression vectors such as pXT1 (as described below in example 30), or by constructing promoter-signal sequence-reporter gene vectors which encode fusion proteins between the signal peptide and an assayable reporter protein. After introduction of these vectors into a suitable host cell, such as COS cells or NIH 3T3 cells, the growth medium may be harvested and analyzed for the presence of the secreted protein. The medium from these cells is compared to the medium from control cells containing vectors lacking the signal sequence or extended cDNA insert to identify vectors which encode a functional signal peptide or an authentic secreted protein.

Those 5' ESTs which encoded a signal peptide, as determined by the method of Example 22 above, were further grouped into four categories based on their homology to known sequences as described in Example 24 below.

#### **EXAMPLE 24**

### 15

20

25

30

10

5

## Categorization of 5' ESTs Encoding a Signal Peptide

Those 5' ESTs having a sequence not matching any known vertebrate sequence nor any publicly available EST sequence were designated "new." Of the sequences in the SignalTag<sup>TM</sup> database, 947 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those 5' ESTs having a sequence not matching any vertebrate sequence but matching a publicly known EST were designated "EST-ext", provided that the known EST sequence was extended by at least 40 nucleotides in the 5' direction. Of the sequences in the SignalTag™ database, 150 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those ESTs not matching any vertebrate sequence but matching a publicly known EST without extending the known EST by at least 40 nucleotides in the 5' direction were designated "EST." Of the sequences in the SignalTag<sup>™</sup> database, 599 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those 5' ESTs matching a human mRNA sequence but extending the known sequence by at least 40 nucleotides in the 5' direction were designated "VERT-ext." Of the sequences in the SignalTag<sup>™</sup> database, 23 of the 5' ESTs having a Von Heijne's score of at

least 3.5 fell into this category. Included in this category was a 5' EST which extended the known sequence of the human translocase mRNA by more than 200 bases in the 5' direction. A 5' EST which extended the sequence of a human tumor suppressor gene in the 5' direction was also identified.

Table V shows the distribution of 5' ESTs in each category and the number of 5' ESTs in each category having a given minimum von Heijne's score.

# 3. Evaluation of Spatial and Temporal Expression of mRNAs Corresponding to the 5'ESTs or Extended cDNAs

10

5

Each of the 5' ESTs was also categorized based on the tissue from which its corresponding mRNA was obtained, as described below in Example 25.

### **EXAMPLE 25**

15

## Categorization of Expression Patterns

Table VI shows the distribution of 5' ESTs in each of the above defined category with respect to the tissue from which the 5'ESTs of the corresponding mRNA were obtained.

Table II provides the sequence identification numbers of 5' EST sequences derived from different tissues, the categories in which these sequences fall, and the von Heijne's score of the signal peptides which they encode. The 5' EST sequences and the amino acid sequences they encode are provided in the appended sequence listings. Table III provides the sequence ID numbers of the 5' ESTs and the sequences of the signal peptides which they encode. The sequences of the 5' ESTs and the polypeptides they encode are provided in the sequence listing appended hereto.

25

30

20

The sequences of DNA SEQ ID NOs: 38-185 can readily be screened for any errors therein and any sequence ambiguities can be resolved by resequencing a fragment containing such errors or ambiguities on both strands. Such fragments may be obtained from the plasmids stored in the inventors' laboratory or can be isolated using the techniques described herein. Resolution of any such ambiguities or errors may be facilitated by using primers which hybridize to sequences located close to the ambiguous or erroneous sequences. For example, the primers may hybridize to sequences within 50-75 bases of the ambiguity or

10

15

20

25

30.

error. Upon resolution of an error or ambiguity, the corresponding corrections can be made in the protein sequences encoded by the DNA containing the error or ambiguity.

In addition to categorizing the 5' ESTs with respect to their tissue of origin, the spatial and temporal expression patterns of the mRNAs corresponding to the 5' ESTs, as well as their expression levels, may be determined as described in Example 26 below. Characterization of the spatial and temporal expression patterns and expression levels of these mRNAs is useful for constructing expression vectors capable of producing a desired level of gene product in a desired spatial or temporal manner, as will be discussed in more detail below.

Furthermore, 5' ESTs whose corresponding mRNAs are associated with disease states may also be identified. For example, a particular disease may result from the lack of expression, over expression, or under expression of an mRNA corresponding to a 5' EST. By comparing mRNA expression patterns and quantities in samples taken from healthy individuals with those from individuals suffering from a particular disease, 5' ESTs responsible for the disease may be identified.

It will be appreciated that the results of the above characterization procedures for 5' ESTs also apply to extended cDNAs (obtainable as described below) which contain sequences adjacent to the 5' ESTs. It will also be appreciated that if desired, characterization may be delayed until extended cDNAs have been obtained rather than characterizing the ESTs themselves.

### **EXAMPLE 26**

## Evaluation of Expression Levels and Patterns of mRNAs

## Corresponding to 5' ESTs or Extended cDNAs

Expression levels and patterns of mRNAs corresponding to 5' ESTs or extended cDNAs (obtainable as described below in example 27) may be analyzed by solution hybridization with long probes as described in International Patent Application No. WO 97/05277, the entire contents of which are hereby incorporated by reference. Briefly, a 5' EST, extended cDNA, or fragment thereof corresponding to the gene encoding the mRNA to be characterized is inserted at a cloning site immediately downstream of a bacteriophage (T3,

10

15

20

25

30

T7 or SP6) RNA polymerase promoter to produce antisense RNA. Preferably, the 5' EST or extended cDNA has 100 or more nucleotides. The plasmid is linearized and transcribed in the presence of ribonucleotides comprising modified ribonucleotides (*i.e.* biotin-UTP and DIG-UTP). An excess of this doubly labeled RNA is hybridized in solution with mRNA isolated from cells or tissues of interest. The hybridizations are performed under standard stringent conditions (40-50°C for 16 hours in an 80% formamide, 0.4 M NaCl buffer, pH 7-8). The unhybridized probe is removed by digestion with ribonucleases specific for single-stranded RNA (*i.e.* RNases CL3, T1, Phy M, U2 or A). The presence of the biotin-UTP modification enables capture of the hybrid on a microtitration plate coated with streptavidin. The presence of the DIG modification enables the hybrid to be detected and quantified by ELISA using an anti-DIG antibody coupled to alkaline phosphatase.

The 5' ESTs, extended cDNAs, or fragments thereof may also be tagged with nucleotide sequences for the serial analysis of gene expression (SAGE) as disclosed in UK Patent Application No. 2 305 241 A, the entire contents of which are incorporated by reference. In this method, cDNAs are prepared from a cell, tissue, organism or other source of nucleic acid for which gene expression patterns must be determined. The resulting cDNAs are separated into two pools. The cDNAs in each pool are cleaved with a first restriction endonuclease, called an anchoring enzyme, having a recognition site which is likely to be present at least once in most cDNAs. The fragments which contain the 5' or 3' most region of the cleaved cDNA are isolated by binding to a capture medium such as streptavidin coated beads. A first oligonucleotide linker having a first sequence for hybridization of an amplification primer and an internal restriction site for a so-called tagging endonuclease is ligated to the digested cDNAs in the first pool. Digestion with the second endonuclease produces short tag fragments from the cDNAs.

A second oligonucleotide having a second sequence for hybridization of an amplification primer and an internal restriction site is ligated to the digested cDNAs in the second pool. The cDNA fragments in the second pool are also digested with the tagging endonuclease to generate short tag fragments derived from the cDNAs in the second pool. The tags resulting from digestion of the first and second pools with the anchoring enzyme and the tagging endonuclease are ligated to one another to produce so-called ditags. In some embodiments, the ditags are concatamenized to produce ligation products containing from 2

10

15

20

25

30

to 200 ditags. The tag sequences are then determined and compared to the sequences of the 5' ESTs or extended cDNAs to determine which 5' ESTs or extended cDNAs are expressed in the cell, tissue, organism, or other source of nucleic acids from which the tags were derived. In this way, the expression pattern of the 5' ESTs or extended cDNAs in the cell, tissue, organism, or other source of nucleic acids is obtained.

Quantitative analysis of gene expression may also be performed using arrays. As used herein, the term array means a one dimensional, two dimensional, or multidimensional arrangement of full length cDNAs (i.e. extended cDNAs which include the coding sequence for the signal peptide, the coding sequence for the mature protein, and a stop codon), extended cDNAs, 5' ESTs or fragments thereof of sufficient length to permit specific detection of gene expression. Preferably, the fragments are at least 15 nucleotides in length. More preferably, the fragments are at least 100 nucleotide long. More preferably, the fragments are more than 100 nucleotides in length. In some embodiments, the fragments may be more than 500 nucleotide long.

For example, quantitative analysis of gene expression may be performed with full length cDNAs as defined below, extended cDNAs, 5' ESTs, or fragments thereof in a complementary DNA microarray as described by Schena et al. (Science 270:467-470, 1995; Proc. Natl. Acad. Sci. U.S.A. 93:10614-10619, 1996). Full length cDNAs, extended cDNAs, 5' ESTs or fragments thereof are amplified by PCR and arrayed from 96-well microtiter plates onto silylated microscope slides using high-speed robotics. Printed arrays are incubated in a humid chamber to allow rehydration of the array elements and rinsed, once in 0.2% SDS for 1 min, twice in water for 1 min and once for 5 min in sodium borohydride solution. The arrays are submerged in water for 2 min at 95°C, transferred into 0.2% SDS for 1 min, rinsed twice with water, air dried and stored in the dark at 25°C.

Cell or tissue mRNA is isolated or commercially obtained and probes are prepared by a single round of reverse transcription. Probes are hybridized to 1 cm<sup>2</sup> microarrays under a 14 x 14 mm glass coverslip for 6-12 hours at 60°C. Arrays are washed for 5 min at 25°C in low stringency wash buffer (1 x SSC/0.2% SDS), then for 10 min at room temperature in high stringency wash buffer (0.1 x SSC/0.2% SDS). Arrays are scanned in 0.1 x SSC using a fluorescence laser scanning device fitted with a custom filter set. Accurate differential

10

15

20

25

expression measurements are obtained by taking the average of the ratios of two independent hybridizations.

Quantitative analysis of the expression of genes may also be performed with full length cDNAs, extended cDNAs, 5' ESTs, or fragments thereof in complementary DNA arrays as described by Pietu et al.. (Genome Research 6:492-503, 1996). The full length cDNAs, extended cDNAs, 5' ESTs or fragments thereof are PCR amplified and spotted on membranes. Then, mRNAs originating from various tissues or cells are labeled with radioactive nucleotides. After hybridization and washing in controlled conditions, the hybridized mRNAs are detected by phospho-imaging or autoradiography. Duplicate experiments are performed and a quantitative analysis of differentially expressed mRNAs is then performed.

Alternatively, expression analysis of the 5' ESTs or extended cDNAs can be done through high density nucleotide arrays as described by Lockhart et al. (Nature Biotechnology 14: 1675-1680, 1996) and Sosnowsky et al. (Proc. Natl. Acad. Sci. 94:1119-1123, 1997). Oligonucleotides of 15-50 nucleotides corresponding to sequences of the 5' ESTs or extended cDNAs are synthesized directly on the chip (Lockhart et al., supra) or synthesized and then addressed to the chip (Sosnowsky et al., supra). Preferably, the oligonucleotides are about 20 nucleotides in length.

cDNA probes labeled with an appropriate compound, such as biotin, digoxigenin or fluorescent dye, are synthesized from the appropriate mRNA population and then randomly fragmented to an average size of 50 to 100 nucleotides. The said probes are then hybridized to the chip. After washing as described in Lockhart et al, supra and application of different electric fields (Sonowsky et al, supra.), the dyes or labeling compounds are detected and quantified. Duplicate hybridizations are performed. Comparative analysis of the intensity of the signal originating from cDNA probes on the same target oligonucleotide in different cDNA samples indicates a differential expression of the mRNA corresponding to the 5' EST or extended cDNA from which the oligonucleotide sequence has been designed.

10

15

20

25

30

# III. Use of 5' ESTs to Clone Extended cDNAs and to Clone the Corresponding Genomic DNAs

Once 5' ESTs which include the 5' end of the corresponding mRNAs have been selected using the procedures described above, they can be utilized to isolate extended cDNAs which contain sequences adjacent to the 5' ESTs. The extended cDNAs may include the entire coding sequence of the protein encoded by the corresponding mRNA, including the authentic translation start site, the signal sequence, and the sequence encoding the mature protein remaining after cleavage of the signal peptide. Such extended cDNAs are referred to herein as "full length cDNAs." Alternatively, the extended cDNAs may include only the sequence encoding the mature protein remaining after cleavage of the signal peptide, or only the sequence encoding the signal peptide.

Example 27 below describes a general method for obtaining extended cDNAs using 5' ESTs. Example 28 below provides experimental results, using the method explained in example 27, describing several extended cDNAs including the entire coding sequence and authentic 5' end of the corresponding mRNA for several secreted proteins.

The methods of Examples 27, 28, and 29 can also be used to obtain extended cDNAs which encode less than the entire coding sequence of the secreted proteins encoded by the genes corresponding to the 5' ESTs. In some embodiments, the extended cDNAs isolated using these methods encode at least 10 amino acids of one of the proteins encoded by the sequences of SEQ ID NOs: 38-185. In further embodiments, the extended cDNAs encode at least 20 amino acids of the proteins encoded by the sequences of SEQ ID NOs: 38-185. In further embodiments, the extended cDNAs encode at least 30 amino amino acids of the sequences of SEQ ID NOs: 38-185. In a preferred embodiment, the extended cDNAs encode a full length protein sequence, which includes the protein coding sequences of SEQ ID NOs: 38-185.

#### **EXAMPLE 27**

# General Method for Using 5' ESTs to Clone and Sequence cDNAs which Include the Entire Coding Region and the Authentic 5' End of the Corresponding mRNA

The following general method has been used to quickly and efficiently isolate extended cDNAs having the authentic 5' ends of their corresponding mRNAs as well as

the full protein coding sequence and including sequence adjacent to the sequences of the 5' ESTs used to obtain them. This method may be applied to obtain extended cDNAs for any 5' EST in the NetGenc™ database, including those 5' ESTs encoding polypeptides belonging to secreted proteins. The method is summarized in figure 3.

5

10

15

20

25

## 1. Obtention of Extended cDNAs

### a) First strand synthesis

The method takes advantage of the known 5' sequence of the mRNA. A reverse transcription reaction is conducted on purified mRNA with a poly 14dT primer containing a 49 nucleotide sequence at its 5' end allowing the addition of a known sequence at the end of the cDNA which corresponds to the 3' end of the mRNA. For example, the primer may have the following sequence: 5'-ATC GTT GAG ACT CGT ACC AGC AGA GTC ACG AGA GAG ACT ACA CGG TAC TGG TTT TTT TTT TTT TTVN -3' (SEQ ID NO:14). Those skilled in the art will appreciate that other sequences may also be added to the poly dT sequence and used to prime the first strand synthesis. Using this primer and a reverse transcriptase such as the Superscript II (Gibco BRL) or Rnase H Minus M-MLV (Promega) enzyme, a reverse transcript anchored at the 3' polyA site of the RNAs is generated.

After removal of the mRNA hybridized to the first cDNA strand by alkaline hydrolysis, the products of the alkaline hydrolysis and the residual poly dT primer are eliminated with an exclusion column such as an AcA34 (Biosepra) matrix as explained in Example 11.

## b) Second strand synthesis

A pair of nested primers on each end is designed based on the known 5' sequence from the 5' EST and the known 3' end added by the poly dT primer used in the first strand synthesis. Softwares used to design primers are either based on GC content and melting temperatures of oligonucleotides, such as OSP (Illier and Green, PCR Meth. Appl. 1:124-128, 1991), or based on the octamer frequency disparity method (Griffais et al., Nucleic Acids Res. 19: 3887-3891, 1991) such as PC-Rare (http://bioinformatics.weizmann.ac.il/software/PC-Rare/doc/manuel.html).

10

15

20

25

Preferably, the nested primers at the 5' end are separated from one another by four to nine bases. The 5' primer sequences may be selected to have melting temperatures and specificities suitable for use in PCR.

Preferably, the nested primers at the 3' end are separated from one another by four to nine bases. For example, the nested 3' primers may have the following sequences: (5'- CCA GCA GAG TCA CGA GAG AGA CTA CAC GG -3'(SEQ ID NO:15), and 5'- CAC GAG AGA GAC TAC ACG GTA CTG G -3' (SEQ ID NO:16). These primers were selected because they have melting temperatures and specificities compatible with their use in PCR. However, those skilled in the art will appreciate that other sequences may also be used as primers.

The first PCR run of 25 cycles is performed using the Advantage Tth Polymerase Mix (Clontech) and the outer primer from each of the nested pairs. A second 20 cycle PCR using the same enzyme and the inner primer from each of the nested pairs is then performed on 1/2500 of the first PCR product. Thereafter, the primers and nucleotides are removed.

## 2. Sequencing of Full Length Extended cDNAs or Fragments Thereof

Due to the lack of position constraints on the design of 5' nested primers compatible for PCR use using the OSP software, amplicons of two types are obtained. Preferably, the second 5' primer is located upstream of the translation initiation codon thus yielding a nested PCR product containing the whole coding sequence. Such a full length extended cDNA undergoes a direct cloning procedure as described in section a. However, in some cases, the second 5' primer is located downstream of the translation initiation codon, thereby yielding a PCR product containing only part of the ORF. Such incomplete PCR products are submitted to a modified procedure described in section b.

a) Nested PCR products containing complete ORFs

When the resulting nested PCR product contains the complete coding sequence, as predicted from the 5'EST sequence, it is cloned in an appropriate vector such as pED6dpc2, as described in section 3.

30 b) Nested PCR products containing incomplete ORFs

10

15

20

25

30

When the amplicon does not contain the complete coding sequence, intermediate steps are necessary to obtain both the complete coding sequence and a PCR product containing the full coding sequence. The complete coding sequence can be assembled from several partial sequences determined directly from different PCR products as described in the following section.

Once the full coding sequence has been completely determined, new primers compatible for PCR use are designed to obtain amplicons containing the whole coding region. However, in such cases, 3' primers compatible for PCR use are located inside the 3' UTR of the corresponding mRNA, thus yielding amplicons which lack part of this region, *i.e.* the polyA tract and sometimes the polyadenylation signal, as illustrated in figure 3. Such full length extended cDNAs are then cloned into an appropriate vector as described in section 3.

## c) Sequencing extended cDNAs

Sequencing of extended cDNAs is performed using a Die Terminator approach with the AmpliTaq DNA polymerase FS kit available from Perkin Elmer.

In order to sequence PCR fragments, primer walking is performed using software such as OSP to choose primers and automated computer software such as ASMG (Sutton et al., Genome Science Technol. 1: 9-19, 1995) to construct contigs of walking sequences including the initial 5' tag using minimum overlaps of 32 nucleotides. Preferably, primer walking is performed until the sequences of full length cDNAs are obtained.

Completion of the sequencing of a given extended cDNA fragment is assessed as follows. Since sequences located after a polyA tract are difficult to determine precisely in the case of uncloned products, sequencing and primer walking processes for PCR products are interrupted when a polyA tract is identified in extended cDNAs obtained as described in case b. The sequence length is compared to the size of the nested PCR product obtained as described above. Due to the limited accuracy of the determination of the PCR product size by gel electrophoresis, a sequence is considered complete if the size of the obtained sequence is at least 70 % the size of the first nested PCR product. If the length of the sequence determined from the computer analysis is not at least 70 % of the length of the nested PCR product, these PCR products are cloned and the sequence of the insertion is determined. When Northern blot data are available, the size of the mRNA detected for a given PCR

10

15

20

25

30

product is used to finally assess that the sequence is complete. Sequences which do not fulfill the above criteria are discarded and will undergo a new isolation procedure.

Sequence data of all extended cDNAs are then transferred to a proprietary database, where quality controls and validation steps are carried out as described in example 15.

## 3. Cloning of Full Length Extended cDNAs

The PCR product containing the full coding sequence is then cloned in an appropriate vector. For example, the extended cDNAs can be cloned into the expression vector pED6dpc2 (DiscoverEase, Genetics Institute, Cambridge, MA) as follows. pED6dpc2 vector DNA is prepared with blunt ends by performing an EcoRI digestion followed by a fill in reaction. The blunt ended vector is dephosphorylated. After removal of PCR primers and ethanol precipitation, the PCR product containing the full coding sequence or the extended cDNA obtained as described above is phosphorylated with a kinase subsequently removed by phenol-Sevag extraction and precipitation. The double stranded extended cDNA is then ligated to the vector and the resulting expression plasmid introduced into appropriate host cells.

Since the PCR products obtained as described above are blunt ended molecules that can be cloned in either direction, the orientation of several clones for each PCR product is determined. Then, 4 to 10 clones are ordered in microtiter plates and subjected to a PCR reaction using a first primer located in the vector close to the cloning site and a second primer located in the portion of the extended cDNA corresponding to the 3' end of the mRNA. This second primer may be the antisense primer used in anchored PCR in the case of direct cloning (case a) or the antisense primer located inside the 3'UTR in the case of indirect cloning (case b). Clones in which the start codon of the extended cDNA is operably linked to the promoter in the vector so as to permit expression of the protein encoded by the extended cDNA are conserved and sequenced. In addition to the ends of cDNA inserts, approximately 50 bp of vector DNA on each side of the cDNA insert are also sequenced.

The cloned PCR products are then entirely sequenced according to the aforementioned procedure. In this case, contigation of long fragments is then performed on walking sequences that have already contigated for uncloned PCR products during

15

20

25

30

primer walking. Sequencing of cloned amplicons is complete when the resulting contigs include the whole coding region as well as overlapping sequences with vector DNA on both ends.

## 5 4. Computer analysis of Full Length Extended cDNA

Sequences of all full length extended cDNAs are then submitted to further analysis as described below. Before searching the extended full length cDNAs for sequences of interest, extended cDNAs which are not of interest (vector RNAs, transfer RNAs, ribosomal RNAs, mitochondrial RNAs, prokaryotic RNAs and fungal RNAs) are discarded using methods essentially similar to those described for 5'ESTs in Example 18.

## a) Identification of structural features

Structural features, e.g. polyA tail and polyadenylation signal, of the sequences of full length extended cDNAs are subsequently determined as follows.

A polyA tail is defined as a homopolymeric stretch of at least 11 A with at most one alternative base within it. The polyA tail search is restricted to the last 100 nt of the sequence and limited to stretches of 11 consecutive A's because sequencing reactions are often not readable after such a polyA stretch. Stretches having more than 90% homology over 8 nucleotides are identified as polyA tails using BLAST2N.

To search for a polyadenylation signal, the polyA tail is clipped from the full-length sequence. The 50 bp preceding the polyA tail are first searched for the canonic polyadenylation AAUAAA signal and, if the canonic signal is not detected, for the alternative AUUAAA signal (Sheets et al., Nuc. Acids Res. 18: 5799-5805, 1990). If neither of these consensus polyadenylation signals is found, the canonic motif is searched again allowing one mismatch to account for possible sequencing errors. More than 85% of identified polyadenylation signals of either type actually ends 10 to 30 bp from the polyA tail. Alternative AUUAAA signals represents approximately 15% of the total number of identified polyadenylation signals.

### b) Identification of functional features

Functional features, e.g. ORFs and signal sequences, of the sequences of full length extended cDNAs were subsequently determined as follows.

10

15.

20

25

30

The 3 upper strand frames of extended cDNAs are searched for ORFs defined as the maximum length fragments beginning with a translation intiation codon and ending with a stop codon. ORFs encoding at least 20 amino acids are preferred.

Each found ORF is then scanned for the presence of a signal peptide in the first 50 amino-acids or, where appropriate, within shorter regions down to 20 amino acids or less in the ORF, using the matrix method of von Heijne (*Nuc. Acids Res.* 14: 4683-4690, 1986), the disclosure of which is incorporated herein by reference as described in Example 22.

c) Homology to either nucleotidic or proteic sequences

Categorization of full-length sequences may be achieved using procedures essentially similar to those described for 5'ESTs in Example 24.

Extended cDNAs prepared as described above may be subsequently engineered to obtain nucleic acids which include desired portions of the extended cDNA using conventional techniques such as subcloning, PCR, or *in vitro* oligonucleotide synthesis. For example, nucleic acids which include only the full coding sequences (*i.e.* the sequences encoding the signal peptide and the mature protein remaining after the signal peptide is cleaved off) may be obtained using techniques known to those skilled in the art. Alternatively, conventional techniques may be applied to obtain nucleic acids which contain only the coding sequences for the mature protein remaining after the signal peptide is cleaved off or nucleic acids which contain only the coding sequences for the signal peptides.

Similarly, nucleic acids containing any other desired portion of the coding sequences for the secreted protein may be obtained. For example, the nucleic acid may contain at least 10 consecutive bases of an extended cDNA such as one of the extended cDNAs described below. In another embodiment, the nucleic acid may contain at least 15 consecutive bases of an extended cDNA such as one of the extended cDNAs described below. Alternatively, the nucleic acid may contain at least 20 consecutive bases of an extended cDNA such as one of the extended cDNAs described below. In another embodiment, the nucleic acid may contain at least 25 consecutive bases of an extended cDNAs uch as one of the extended cDNAs described below. In yet another embodiment, the nucleic acid may contain at least 40 described below. In yet another embodiment, the nucleic acid may contain at least 40

consecutive bases of an extended cDNA such as one of the extended cDNAs described below.

Once an extended cDNA has been obtained, it can be sequenced to determine the amino acid sequence it encodes. Once the encoded amino acid sequence has been determined, one can create and identify any of the many conceivable cDNAs that will encode that protein by simply using the degeneracy of the genetic code. For example, allelic variants or other homologous nucleic acids can be identified as described below. Alternatively, nucleic acids encoding the desired amino acid sequence can be synthesized *in vitro*.

In a preferred embodiment, the coding sequence may be selected using the known codon or codon pair preferences for the host organism in which the cDNA is to be expressed.

The extended cDNAs derived from the 5' ESTS of the present invention were obtained as described in Example 28 below.

#### **EXAMPLE 28**

15

20

25

30

10

5

## Characterization of cloned extended cDNAs obtained using 5' ESTs

The procedure described in Example 27 above was used to obtain the extended cDNAs derived from the 5' ESTs of the present invention in a variety of tissues. The following list provides a few examples of thus obtained extended cDNAs.

Using this approach, the full length cDNA of SEQ ID NO:17 (internal identification number 48-19-3-G1-FL1) was obtained. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MKKVLLLITAILAVAVG (SEQ ID NO: 18) having a von Heijne score of 8.2.

The full length cDNA of SEQ ID NO:19 (internal identification number 58-34-2-E7-FL2) was also obtained using this procedure. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MWWFQQGLSFLPSALVIWTSA (SEQ ID NO:20) having a von Heijne score of 5.5.

Another full length cDNA obtained using the procedure described above has the sequence of SEQ ID NO:21 (internal identification number 51-27-1-E8-FL1). This cDNA, falls into the "EST-ext" category described above and encodes the signal peptide MVLTTLPSANSANSPVNMPTTGPNSLSYASSALSPCLT (SEQ ID NO:22) having a von Heijne score of 5.9.

10

15

20

25

30

The above procedure was also used to obtain a full length cDNA having the sequence of SEQ ID NO:23 (internal identification number 76-4-1-G5-FL1). This cDNA falls into the "EST-ext" category described above and encodes the signal peptide ILSTVTALTFAXA (SEQ ID NO:24) having a von Heijne score of 5.5.

The full length cDNA of SEQ ID NO:25 (internal identification number 51-3-3-B10-FL3) was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal peptide LVLTLCTLPLAVA (SEQ ID NO:26) having a von Heijne score of 10.1.

The full length cDNA of SEQ ID NO:27 (internal identification number 58-35-2-F10-FL2) was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal peptide LWLLFFLVTAIHA (SEQ ID NO:28) having a von Heijne score of 10.7.

Bacterial clones containing plasmids containing the full length cDNAs described above are presently stored in the inventor's laboratories under the internal identification numbers provided above. The inserts may be recovered from the stored materials by growing an aliquot of the appropriate bacterial clone in the appropriate medium. The plasmid DNA can then be isolated using plasmid isolation procedures familiar to those skilled in the art such as alkaline lysis minipreps or large scale alkaline lysis plasmid isolation procedures. If desired the plasmid DNA may be further enriched by centrifugation on a cesium chloride gradient, size exclusion chromatography, or anion exchange chromatography. The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the cDNA insertion. The PCR product which corresponds to the cDNA can then be manipulated using standard cloning techniques familiar to those skilled in the art.

The polypeptides encoded by the extended cDNAs may be screened for the presence of known structural or functional motifs or for the presence of signatures, small amino acid sequences which are well conserved amongst the members of a protein family. The conserved regions have been used to derive consensus patterns or matrices included in the PROSITE data bank, in particular in the file prosite.dat (Release 13.0 of November 1995, located at <a href="http://expasy.hcuge.ch/sprot/prosite.html">http://expasy.hcuge.ch/sprot/prosite.html</a>. Prosite convert and prosite scan

10

15

programs (http://ulrec3.unil.ch/ftpserveur/prosite\_scan) may be used to find signatures on the extended cDNAs.

For each pattern obtained with the prosite\_convert program from the prosite.dat file, the accuracy of the detection on a new protein sequence may be assessed by evaluating the frequency of irrelevant hits on the population of human secreted proteins included in the data bank SWISSPROT. The ratio between the number of hits on shuffled proteins (with a window size of 20 amino acids) and the number of hits on native (unshuffled) proteins may be used as an index. Every pattern for which the ratio is greater than 20% (one hit on shuffled proteins for 5 hits on native proteins) may be skipped during the search with prosite\_scan. The program used to shuffle protein sequences (db\_shuffled) and the program used to determine the statistics for each pattern in the protein data banks (prosite\_statistics) are available on the ftp site <a href="http://ulrec3.unil.ch/ftpserveur/prosite\_scan">http://ulrec3.unil.ch/ftpserveur/prosite\_scan</a>.

In addition to PCR based methods for obtaining extended cDNAs, traditional hybridization based methods may also be employed. These methods may also be used to obtain the genomic DNAs which encode the mRNAs from which the 5' ESTs were derived, mRNAs corresponding to the extended cDNAs, or nucleic acids which are homologous to extended cDNAs or 5' ESTs. Example 29 below provides examples of such methods.

20

25

30

### **EXAMPLE 29**

# Methods for Obtaining cDNAs which include the Entire Coding Region and the Authentic 5'End of the Corresponding mRNA

A full length cDNA library can be made using the strategies described in Examples 13, 14, 15, and 16 above by replacing the random nonamer used in Example 14 with an oligo-dT primer. For instance, the oligonucleotide of SEQ ID NO:14 may be used.

Alternatively, a cDNA library or genomic DNA library may be obtained from a commercial source or made using techniques familiar to those skilled in the art. Such cDNA or genomic DNA librairies may be used to isolate extended cDNAs obtained from 5' EST or nucleic acids homologous to extended cDNAs or 5' EST as follows. The cDNA library or genomic DNA library is hybridized to a detectable probe comprising at least 10 consecutive nucleotides from the 5' EST or extended cDNA using conventional techniques. Preferably,

10

15

20

25

the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises at least 20 to 30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST or extended cDNA.

Techniques for identifying cDNA clones in a cDNA library which hybridize to a given probe sequence are disclosed in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989, the disclosure of which is incorporated herein by reference. The same techniques may be used to isolate genomic DNAs.

Briefly, cDNA or genomic DNA clones which hybridize to the detectable probe are identified and isolated for further manipulation as follows. A probe comprising at least 10 consecutive nucleotides from the 5' EST or extended cDNA is labeled with a detectable label such as a radioisotope or a fluorescent molecule. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises 20 to 30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST or extended cDNA.

Techniques for labeling the probe are well known and include phosphorylation with polynucleotide kinase, nick translation, *in vitro* transcription, and non radioactive techniques. The cDNAs or genomic DNAs in the library are transferred to a nitrocellulose or nylon filter and denatured. After blocking of non specific sites, the filter is incubated with the labeled probe for an amount of time sufficient to allow binding of the probe to cDNAs or genomic DNAs containing a sequence capable of hybridizing thereto.

By varying the stringency of the hybridization conditions used to identify extended cDNAs or genomic DNAs which hybridize to the detectable probe, extended cDNAS having different levels of homology to the probe can be identified and isolated as described below.

10

15

**20** ·

25

30

# 1. Identification of Extended cDNA or Genomic cDNA Sequences Having a High Degree of Homology to the Labeled Probe

To identify extended cDNAs or genomic DNAs having a high degree of homology to the probe sequence, the melting temperature of the probe may be calculated using the following formulas:

For probes between 14 and 70 nucleotides in length the melting temperature (Tm) is calculated using the formula: Tm=81.5+16.6(log [Na+])+0.41(fraction G+C)-(600/N) where N is the length of the probe.

If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation Tm=81.5+16.6(log [Na+])+0.41(fraction G+C)-(0.63% formamide)-(600/N) where N is the length of the probe.

Prehybridization may be carried out in 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 µg denatured fragmented salmon sperm DNA or 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 µg denatured fragmented salmon sperm DNA, 50% formamide. The formulas for SSC and Denhardt's solutions are listed in Sambrook *et al.*, *supra*.

Hybridization is conducted by adding the detectable probe to the prehybridization solutions listed above. Where the probe comprises double stranded DNA, it is denatured before addition to the hybridization solution. The filter is contacted with the hybridization solution for a sufficient period of time to allow the probe to hybridize to extended cDNAs or genomic DNAs containing sequences complementary thereto or homologous thereto. For probes over 200 nucleotides in length, the hybridization may be carried out at 15-25°C below the Tm. For shorter probes, such as oligonucleotide probes, the hybridization may be conducted at 15-25°C below the Tm. Preferably, for hybridizations in 6X SSC, the hybridization is conducted at approximately 68°C. Preferably, for hybridizations in 50% formamide containing solutions, the hybridization is conducted at approximately 42°C.

All of the foregoing hybridizations would be considered to be under "stringent" conditions.

Following hybridization, the filter is washed in 2X SSC, 0.1% SDS at room temperature for 15 minutes. The filter is then washed with 0.1X SSC, 0.5% SDS at room temperature for 30 minutes to 1 hour. Thereafter, the solution is washed at the hybridization

10

15

20

25

30

temperature in 0.1X SSC, 0.5% SDS. A final wash is conducted in 0.1X SSC at room temperature.

Extended cDNAs, nucleic acids homologous to extended cDNAs or 5' ESTs, or genomic DNAs which have hybridized to the probe are identified by autoradiography or other conventional techniques.

## 2. Obtention of Extended cDNA or Genomic cDNA Sequences Having Lower Degrees of Homology to the Labeled Probe

The above procedure may be modified to identify extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs having decreasing levels of homology to the probe sequence. For example, to obtain extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs of decreasing homology to the detectable probe, less stringent conditions may be used. For example, the hybridization temperature may be decreased in increments of 5°C from 68°C to 42°C in a hybridization buffer having a sodium concentration of approximately 1M. Following hybridization, the filter may be washed with 2X SSC, 0.5% SDS at the temperature of hybridization. These conditions are considered to be "moderate" conditions above 50°C and "low" conditions below 50°C.

Alternatively, the hybridization may be carried out in buffers, such as 6X SSC, containing formamide at a temperature of 42°C. In this case, the concentration of formamide in the hybridization buffer may be reduced in 5% increments from 50% to 0% to identify clones having decreasing levels of homology to the probe. Following hybridization, the filter may be washed with 6X SSC, 0.5% SDS at 50°C. These conditions are considered to be "moderate" conditions above 25% formamide and "low" conditions below 25% formamide.

Extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs which have hybridized to the probe are identified by autoradiography.

## 3. Determination of the Degree of Homology Between the Obtained Extended cDNAs and the Labeled Probe

If it is desired to obtain nucleic acids homologous to extended cDNAs, such as allelic variants thereof or nucleic acids encoding proteins related to the proteins encoded by the extended cDNAs, the level of homology between the hybridized nucleic acid and the

10

15

20

25

30

extended cDNA or 5' EST used as the probe may be further determined using BLAST2N; parameters may be adapted depending on the sequence length and degree of homology studied. To determine the level of homology between the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived, the nucleotide sequences of the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived are compared. For example, using the above methods, nucleic acids having at least 95% nucleic acid homology to the extended cDNA or 5'EST from which the probe was derived may be obtained and identified. Similarly, by using progressively less stringent hybridization conditions one can obtain and identify nucleic acids having at least 90%, at least 85%, at least 80% or at least 75% homology to the extended cDNA or 5'EST from which the probe was derived.

To determine whether a clone encodes a protein having a given amount of homology to the protein encoded by the extended cDNA or 5' EST, the amino acid sequence encoded by the extended cDNA or 5' EST is compared to the amino acid sequence encoded by the hybridizing nucleic acid. Homology is determined to exist when an amino acid sequence in the extended cDNA or 5' EST is closely related to an amino acid sequence in the hybridizing nucleic acid. A sequence is closely related when it is identical to that of the extended cDNA or 5' EST or when it contains one or more amino acid substitutions therein in which amino acids having similar characteristics have been substituted for one another. Using the above methods and algorithms such as FASTA with parameters depending on the sequence length and degree of homology studied, one can obtain nucleic acids encoding proteins having at least 95%, at least 90%, at least 85%, at least 80% or at least 75% homology to the proteins encoded by the extended cDNA or 5'EST from which the probe was derived.

In addition to the above described methods, other protocols are available to obtain extended cDNAs using 5' ESTs as outlined in the following paragraphs.

Extended cDNAs may be prepared by obtaining mRNA from the tissue, cell, or organism of interest using mRNA preparation procedures utilizing polyA selection procedures or other techniques known to those skilled in the art. A first primer capable of hybridizing to the polyA tail of the mRNA is hybridized to the mRNA and a reverse transcription reaction is performed to generate a first cDNA strand.

10

15

20

25

30

The first cDNA strand is hybridized to a second primer containing at least 10 consecutive nucleotides of the sequences of SEQ ID NOs 38-185. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the sequences of SEQ ID NOs 38-185. More preferably, the primer comprises 20 to 30 consecutive nucleotides from the sequences of SEQ ID NOs 38-185. In some embodiments, the primer comprises more than 30 nucleotides from the sequences of SEQ ID NOs 38-185. If it is desired to obtain extended cDNAs containing the full protein coding sequence, including the authentic translation initiation site, the second primer used contains sequences located upstream of the translation initiation site. The second primer is extended to generate a second cDNA strand complementary to the first cDNA strand. Alternatively, RT-PCR may be performed as described above using primers from both ends of the cDNA to be obtained.

Extended cDNAs containing 5' fragments of the mRNA may be prepared by hybridizing an mRNA comprising the sequence of the 5'EST for which an extended cDNA is desired with a primer comprising at least 10 consecutive nucleotides of the sequences complementary to the 5'EST and reverse transcribing the hybridized primer to make a first cDNA strand from the mRNAs. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the 5'EST. More preferably, the primer comprises 20 to 30 consecutive nucleotides from the 5'EST.

Thereafter, a second cDNA strand complementary to the first cDNA strand is synthesized. The second cDNA strand may be made by hybridizing a primer complementary to sequences in the first cDNA strand to the first cDNA strand and extending the primer to generate the second cDNA strand.

The double stranded extended cDNAs made using the methods described above are isolated and cloned. The extended cDNAs may be cloned into vectors such as plasmids or viral vectors capable of replicating in an appropriate host cell. For example, the host cell may be a bacterial, mammalian, avian, or insect cell.

Techniques for isolating mRNA, reverse transcribing a primer hybridized to mRNA to generate a first cDNA strand, extending a primer to make a second cDNA strand complementary to the first cDNA strand, isolating the double stranded cDNA and cloning the double stranded cDNA are well known to those skilled in the art and are described in Current Protocols in Molecular Biology, John Wiley and Sons, Inc. 1997 and Sambrook et al.,

10

15

20

25

30

Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989, the entire disclosures of which are incorporated herein by reference.

Alternatively, procedures such as the one described in Example 29 may be used for obtaining full length cDNAs or extended cDNAs. In this approach, full length or extended cDNAs are prepared from mRNA and cloned into double stranded phagemids as follows. The cDNA library in the double stranded phagemids is then rendered single stranded by treatment with an endonuclease, such as the Gene II product of the phage F1, and an exonuclease (Chang et al., Gene 127:95-8, 1993). A biotinylated oligonucleotide comprising the sequence of a 5' EST, or a fragment containing at least 10 nucleotides thereof, is hybridized to the single stranded phagemids. Preferably, the fragment comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST. More preferably, the fragment comprises 20-30 consecutive nucleotides from the 5' EST. In some procedures, the fragment may comprise more than 30 consecutive nucleotides from the 5' EST.

Hybrids between the biotinylated oligonucleotide and phagemids having inserts containing the 5' EST sequence are isolated by incubating the hybrids with streptavidin coated paramagnetic beads and retrieving the beads with a magnet (Fry et al., Biotechniques, 13: 124-131, 1992). Therafter, the resulting phagemids containing the 5' EST sequence are released from the beads and converted into double stranded DNA using a primer specific for the 5' EST sequence. Alternatively, protocoles such as the Gene Trapper kit (Gibco BRL) may be used. The resulting double stranded DNA is transformed into bacteria. Extended cDNAs containing the 5' EST sequence are identified by colony PCR or colony hybridization.

Using any of the above described methods in section III, a plurality of extended cDNAs containing full length protein coding sequences or sequences encoding only the mature protein remaining after the signal peptide is cleaved off may be provided as cDNA libraries for subsequent evaluation of the encoded proteins or use in diagnostic assays as described below.

## IV. Expression of Proteins Encoded by Extended cDNAs Isolated Using 5' ESTs

Extended cDNAs containing the full protein coding sequences of their corresponding mRNAs or portions thereof, such as cDNAs encoding the mature protein, may be used to

express the encoded secreted proteins or portions thereof as described in Example 30 below. If desired, the extended cDNAs may contain the sequences encoding the signal peptide to facilitate secretion of the expressed protein. It will be appreciated that a plurality of extended cDNAs containing the full protein coding sequences or portions thereof may be simultaneously cloned into expression vectors to create an expression library for analysis of the encoded proteins as described below.

#### **EXAMPLE 30**

## Expression of the Proteins Encoded by the Genes Corresponding to 5'ESTS or Portions Thereof

10

15

20

25

30

5

To express the proteins encoded by the genes corresponding to 5' ESTs (or portions thereof), full length cDNAs containing the entire protein coding region or extended cDNAs containing sequences adjacent to the 5' ESTs (or portions thereof) are obtained as described in Examples 27-29 and cloned into a suitable expression vector. If desired, the nucleic acids may contain the sequences encoding the signal peptide to facilitate secretion of the expressed protein. The nucleic acids inserted into the expression vectors may also contain sequences upstream of the sequences encoding the signal peptide, such as sequences which regulate expression levels or sequences which confer tissue specific expression.

The nucleic acid encoding the protein or polypeptide to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector may be any of the mammalian, yeast, insect or bacterial expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon context and codon pairing of the sequence may be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, *et al.*, U.S. Patent No. 5,082,767, incorporated herein by this reference.

The cDNA cloned into the expression vector may encode the entire protein (i.e. the signal peptide and the mature protein), the mature protein (i.e. the protein created by cleaving the signal peptide off), only the signal peptide or any other portion thereof.

10

15

20

25

30

The following is provided as one exemplary method to express the proteins encoded by the extended cDNAs corresponding to the 5' ESTs or the nucleic acids described above. First, the methionine initiation codon for the gene and the polyA signal of the gene are identified. If the nucleic acid encoding the polypeptide to be expressed lacks a methionine to serve as the initiation site, an initiating methionine can be introduced next to the first codon of the nucleic acid using conventional techniques. Similarly, if the extended cDNA lacks a polyA signal, this sequence can be added to the construct by, for example, splicing out the polyA signal from pSG5 (Stratagene) using BglII and SalI restriction endonuclease enzymes and incorporating it into the mammalian expression vector pXT1 (Stratagene). pXT1 contains the LTRs and a portion of the gag gene from Moloney Murine Leukemia Virus. The position of the LTRs in the construct allow efficient stable transfection. The vector includes the Herpes Simplex thymidine kinase promoter and the selectable neomycin gene. The extended cDNA or portion thereof encoding the polypeptide to be expressed is obtained by PCR from the bacterial vector using oligonucleotide primers complementary to the extended cDNA or portion thereof and containing restriction endonuclease sequences for Pst I incorporated into the 5'primer and BellI at the 5' end of the corresponding cDNA 3' primer, taking care to ensure that the extended cDNA is positioned with the poly A signal. The purified fragment obtained from the resulting PCR reaction is digested with PstI, blunt ended with an exonuclease, digested with Bgl II, purified and ligated to pXT1 containing a poly A signal and prepared for this ligation (blunt/BgIII).

The ligated product is transfected into mouse NIH 3T3 cells using Lipofectin (Life Technologies, Inc., Grand Island, New York) under conditions outlined in the product specification. Positive transfectants are selected after growing the transfected cells in 600 µg/ml G418 (Sigma, St. Louis, Missouri). Preferably the expressed protein is released into the culture medium, thereby facilitating purification.

Alternatively, the extended cDNAs may be cloned into pED6dpc2 as described above. The resulting pED6dpc2 constructs may be transfected into a suitable host cell, such as COS 1 cells. Methotrexate resistant cells are selected and expanded. Preferably, the protein expressed from the extended cDNA is released into the culture medium thereby facilitating purification.

10

15

20

25

30

Proteins in the culture medium are separated by gel electrophoresis. If desired, the proteins may be ammonium sulfate precipitated or separated based on size or charge prior to electrophoresis.

As a control, the expression vector lacking a cDNA insert is introduced into host cells or organisms and the proteins in the medium are harvested. The secreted proteins present in the medium are detected using techniques familiar to those skilled in the art such as Coomassie blue or silver staining or using antibodies against the protein encoded by the extended cDNA

Antibodies capable of specifically recognizing the protein of interest may be generated using synthetic 15-mer peptides having a sequence encoded by the appropriate 5' EST, extended cDNA, or portion thereof. The synthetic peptides are injected into mice to generate antibody to the polypeptide encoded by the 5' EST, extended cDNA, or portion thereof.

Secreted proteins from the host cells or organisms containing an expression vector which contains the extended cDNA derived from a 5' EST or a portion thereof are compared to those from the control cells or organism. The presence of a band in the medium from the cells containing the expression vector which is absent in the medium from the control cells indicates that the extended cDNA encodes a secreted protein. Generally, the band corresponding to the protein encoded by the extended cDNA will have a mobility near that expected based on the number of amino acids in the open reading frame of the extended cDNA. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

Alternatively, if the protein expressed from the above expression vectors does not contain sequences directing its secretion, the proteins expressed from host cells containing an expression vector with an insert encoding a secreted protein or portion thereof can be compared to the proteins expressed in control host cells containing the expression vector without an insert. The presence of a band in samples from cells containing the expression vector with an insert which is absent in samples from cells containing the expression vector without an insert indicates that the desired protein or portion thereof is being expressed. Generally, the band will have the mobility expected for the secreted protein or portion thereof. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

10

15

20

25

30

The protein encoded by the extended cDNA may be purified using standard immunochromatography techniques. In such procedures, a solution containing the secreted protein, such as the culture medium or a cell extract, is applied to a column having antibodies against the secreted protein attached to the chromatography matrix. The secreted protein is allowed to bind the immunochromatography column. Thereafter, the column is washed to remove non-specifically bound proteins. The specifically bound secreted protein is then released from the column and recovered using standard techniques.

If antibody production is not possible, the extended cDNA sequence or portion thereof may be incorporated into expression vectors designed for use in purification schemes employing chimeric polypeptides. In such strategies, the coding sequence of the extended cDNA or portion thereof is inserted in frame with the gene encoding the other half of the chimera. The other half of the chimera may be  $\beta$ -globin or a nickel binding polypeptide. A chromatography matrix having antibody to  $\beta$ -globin or nickel attached thereto is then used to purify the chimeric protein. Protease cleavage sites may be engineered between the  $\beta$ -globin gene or the nickel binding polypeptide and the extended cDNA or portion thereof. Thus, the two polypeptides of the chimera may be separated from one another by protease digestion.

One useful expression vector for generating β-globin chimerics is pSG5 (Stratagene), which encodes rabbit β-globin. Intron II of the rabbit β-globin gene facilitates splicing of the expressed transcript, and the polyadenylation signal incorporated into the construct increases the level of expression. These techniques as described are well known to those skilled in the art of molecular biology. Standard methods are published in methods texts such as Davis *et al.*, (*Basic Methods in Molecular Biology*, Davis, Dibner, and Battey, ed., Elsevier Press, NY, 1986) and many of the methods are available from Stratagene, Life Technologies, Inc., or Promega. Polypeptide may additionally be produced from the construct using *in vitro* translation systems such as the *In vitro* Express<sup>TM</sup> Translation Kit (Stratagene).

Following expression and purification of the secreted proteins encoded by the 5' ESTs, extended cDNAs, or fragments thereof, the purified proteins may be tested for the ability to bind to the surface of various cell types as described in Example 31 below. It will be appreciated that a plurality of proteins expressed from these cDNAs may be included in a

10

15

20

panel of proteins to be simultaneously evaluated for the activities specifically described below, as well as other biological roles for which assays for determining activity are available.

### **EXAMPLE 31**

## Analysis of Secreted Proteins to Determine Whether they Bind to the Cell Surface

The proteins encoded by the 5' ESTs, extended cDNAs, or fragments thereof are cloned into expression vectors such as those described in Example 30. The proteins are purified by size, charge, immunochromatography or other techniques familiar to those skilled in the art. Following purification, the proteins are labeled using techniques known to those skilled in the art. The labeled proteins are incubated with cells or cell lines derived from a variety of organs or tissues to allow the proteins to bind to any receptor present on the cell surface. Following the incubation, the cells are washed to remove non-specifically bound protein. The labeled proteins are detected by autoradiography. Alternatively, unlabeled proteins may be incubated with the cells and detected with antibodies having a detectable label, such as a fluorescent molecule, attached thereto.

Specificity of cell surface binding may be analyzed by conducting a competition analysis in which various amounts of unlabeled protein are incubated along with the labeled protein. The amount of labeled protein bound to the cell surface decreases as the amount of competitive unlabeled protein increases. As a control, various amounts of an unlabeled protein unrelated to the labeled protein is included in some binding reactions. The amount of labeled protein bound to the cell surface does not decrease in binding reactions containing increasing amounts of unrelated unlabeled protein, indicating that the protein encoded by the cDNA binds specifically to the cell surface.

As discussed above, secreted proteins have been shown to have a number of important physiological effects and, consequently, represent a valuable therapeutic resource. The secreted proteins encoded by the extended cDNAs or portions thereof made according to Examples 27-29 may be evaluated to determine their physiological activities as described below.

25

30

#### **EXAMPLE 32**

# Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Cytokine, Cell Proliferation or Cell Differentiation Activity

As discussed above, secreted proteins may act as cytokines or may affect cellular proliferation or differentiation. Many protein factors discovered to date, including all known 5 cytokines, have exhibited activity in one or more factor dependent cell proliferation assays. and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein encoded by the extended cDNAs is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M (preB M), 2E8, RB5, DA1, 123, T1165. 10 HT2, CTLL2, TF-1, Mo7c and CMK. The proteins encoded by the above extended cDNAs or portions thereof may be evaluated for their ability to regulate T cell or thymocyte proliferation in assays such as those described above or in the following references, which are incorporated herein by reference: Current Protocols in Immunology, Ed. by Coligan et al., Greene Publishing Associates and Wiley-Interscience; Takai et al. J. Immunol. 137:3494-3500, 1986., Bertagnolli et al., J. Immunol. 145:1706-1712, 1990., Bertagnolli et al., Cell. Immunol. 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152:1756-1761, 1994.

In addition, numerous assays for cytokine production and/or the proliferation of spleen cells, lymph node cells and thymocytes are known. These include the techniques disclosed in *Current Protocols in Immunology*, supra 1:3.12.1-3.12.14; and Schreiber In *Current Protocols in Immunology*, supra 1:6.8.1-6.8.8.

The proteins encoded by the cDNAs may also be assayed for the ability to regulate the proliferation and differentiation of hematopoietic or lymphopoietic cells. Many assays for such activity are familiar to those skilled in the art, including the assays in the following references, which are incorporated herein by reference: Bottomly et al., In Current Protocols in Immunology., supra. 1: 6.3.1-6.3.12,; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 36:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Nordan, R., In Current Protocols in Immunology., supra. 1: 6.6.1-6.6.5; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Bennett et al., in

10

15

Current Protocols in Immunology supra 1: 6.15.1; Ciarletta et al., In Current Protocols in Immunology, supra 1: 6.13.1.

The proteins encoded by the cDNAs may also be assayed for their ability to regulate T-cell responses to antigens. Many assays for such activity are familiar to those skilled in the art, including the assays described in the following references, which are incorporated herein by reference: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function), Chapter 6 (Cytokines and Their Cellular Receptors) and Chapter 7, (Immunologic Studies in Humans) in Current Protocols in Immunology supra; Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Those proteins which exhibit cytokine, cell proliferation, or cell differentiation activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which induction of cell proliferation or differentiation is beneficial. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 33**

20

25

30

# Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Activity as Immune System Regulators

The proteins encoded by the cDNAs may also be evaluated for their effects as immune regulators. For example, the proteins may be evaluated for their activity to influence thymocyte or splenocyte cytotoxicity. Numerous assays for such activity are familiar to those skilled in the art including the assays described in the following references, which are incorporated herein by reference: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function 3.1-3.19) and Chapter 7 (Immunologic studies in Humans) in Current Protocols in Immunology, Coligan et al., Eds, Greene Publishing Associates and Wiley-Interscience; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988;

10

15

20

25

30

Bowman et al., J. Virology 61:1992-1998; Bertagnolli et al., Cell. Immunol. 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

The proteins encoded by the cDNAs may also be evaluated for their effects on T-cell dependent immunoglobulin responses and isotype switching. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Maliszewski, *J. Immunol.* 144:3028-3033, 1990; Mond *et al.* in *Current Protocols in Immunology*, 1:3.8.1-3.8.16, *supra*.

The proteins encoded by the cDNAs may also be evaluated for their effect on immune effector cells, including their effect on Th1 cells and cytotoxic lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function 3.1-3.19) and Chapter 7 (Immunologic Studies in Humans) in Current Protocols in Immunology, supra; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

The proteins encoded by the cDNAs may also be evaluated for their effect on dendritic cell mediated activation of naive T-cells. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., J. Exp. Med. 173:549-559, 1991; Macatonia et al., J. Immunol. 154:5071-5079, 1995; Porgador et al.J. Exp. Med 182:255-260, 1995; Nair et al., J. Virol. 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al.J. Exp. Med 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., J. Exp. Med 172:631-640, 1990.

The proteins encoded by the cDNAs may also be evaluated for their influence on the lifetime of lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Res. 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, J. Immunol. 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., Int. J. Oncol. 1:639-648, 1992.

10

15

20

25

30

The proteins encoded by the cDNAs may also be evaluated for their influence on early steps of T-cell commitment and development. Numerous assays for such activity are familiar to those skilled in the art, including without limitation the assays disclosed in the following references, which are incorporated herein by references: Antica et al., Blood 84:111-117, 1994; Fine et al., Cell. Immunol. 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Those proteins which exhibit activity as immune system regulators activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of immune activity is beneficial. For example, the protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., plamodium and various fungal infections such as candidiasis. Of course, in this regard, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Alternatively, proteins encoded by extended cDNAs derived from the 5' ESTs of the present invention may be used in treatment of autoimmune disorders including, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention.

10

15

20

25

30

Using the proteins of the invention it may also be possible to regulate immune responses either up or down.

Down regulation may involve inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T-cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active non-antigen-specific process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after the end of exposure to the tolerizing agent. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions, such as, for example, B7 costimulation), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation, can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve

10

15

20

25

30

sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792, 1992 and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105, 1992. In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor/ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which potentially involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/pr/pr mice or NZB hybrid mice, murine autoimmuno collagen arthritis, diabetes mellitus in OD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., supra, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may involve either enhancing an existing immune response or eliciting an initial immune response as shown by the following examples. For instance, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases

10

15

20

25

30

of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory form of B lymphocyte antigens systemically.

Alternatively, antiviral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells *in vitro* with viral antigen-pulsed APCs either expressing a peptide encoded by extended cDNAs derived from the 5' ESTs of the present invention or together with a stimulatory form of a soluble peptide encoded by extended cDNAs derived from the 5' ESTs of the present invention and reintroducing the *in vitro* primed T cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to T cells *in vivo*, thereby activating the T cells.

In another application, upregulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide encoded by extended cDNAs derived from the 5' ESTs of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide encoded by extended cDNAs derived from the 5' ESTs of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules can be transfected with nucleic acids encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain and  $\beta_2$  microglobulin or an MHC class II  $\alpha$  chain and an MHC class II  $\beta$  chain to thereby express MHC class I or MHC class II proteins on the cell surface, respectively. Expression of the appropriate MHC class I or class II

10

20

25

30

molecules in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject. Alternatively, as described in more detail below, genes encoding these immune system regulator proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 34**

## Assaying the Proteins Expressed from Extended cDNAs

15 <u>or Portions Thereof for Hematopoiesis Regulating Activity</u>

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their hematopoiesis regulating activity. For example, the effect of the proteins on embryonic stem cell differentiation may be evaluated. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Johansson et al. Cell. Biol. 15:141-151, 1995; Keller et al., Mol. Cell. Biol. 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their influence on the lifetime of stem cells and stem cell differentiation. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Freshney, Methylcellulose Colony Forming Assays, in Culture of Hematopoietic Cells., Freshney, et al.. Eds. pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; McNiece and Briddell, in Culture of Hematopoietic Cells, supra; Neben et al., Exp. Hematol. 22:353-359, 1994; Ploemacher and Cobblestone In

10

15

20

25

Culture of Hematopoietic Cells, supral-21, Spooncer et al, in Culture of Hematopoietic Cells, supral 63-179 and Sutherland in Culture of Hematopoietic Cells, supral 139-162.

Those proteins which exhibit hematopoiesis regulatory activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of hematopoeisis is beneficial, such as in the treatment of myeloid or lymphoid cell deficiencies. Involvement in regulating hematopoiesis is indicated even by marginal biological activity in support of colony forming cells or of factor-dependent cell lines. For example, proteins supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, indicates utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells. Proteins supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) may be useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelosuppression. Proteins supporting the growth and proliferation of megakaryocytes and consequently of platelets allows prevention or treatment of various platelet disorders such as thrombocytopenia, and generally may be used in place of or complementary to platelet transfusions. Proteins supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells may therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantion, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in vivo or ex vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy. Alternatively, as described in more detail below, genes encoding hematopoiesis regulating activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

10

15

20

25

30

#### **EXAMPLE 35**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Tissue Growth

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effect on tissue growth. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in International Patent Publication No. WO95/16035, International Patent Publication No. WO95/05846 and International Patent Publication No. WO91/07491, which are incorporated herein by reference.

Assays for wound healing activity include, without limitation, those described in: Winter, *Epidermal Wound Healing*, pps. 71-112, Maibach and Rovee, eds., Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, *J. Invest. Dermatol.* 71:382-84, 1978, which are incorporated herein by reference.

Those proteins which are involved in the regulation of tissue growth may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of tissue growth is beneficial. For example, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. *De novo* bone synthesis induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of bone-forming cell progenitors. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or

10

15

20

25

30

by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein encoded by extended cDNAs derived from the 5' ESTs of the present invention is tendon/ligament formation. A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues. and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition encoded by extended cDNAs derived from the 5' ESTs of the present invention contributes to the repair of tendon or ligaments defects of congenital traumatic or other origin and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions encoded by extended cDNAs derived from the 5' ESTs of the present invention may provide an environment to attract tendon- or ligamentforming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e., for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and

10

15

20

25

Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium) muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to generate. A protein of the invention may also exhibit angiogenic activity.

A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokinc damage.

A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Alternatively, as described in more detail below, genes encoding tissue growth regulating activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

### **EXAMPLE 36**

Assaying the Proteins Expressed from Extended cDNAs or Portions

Thereof for Regulation of Reproductive Hormones

10

15

20

25

30

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their ability to regulate reproductive hormones, such as follicle stimulating hormone. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Vale et al., Endocrinol. 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986, Chapter 6.12 in Current Protocols in Immunology, Coligan et al. Eds. Greene Publishing Associates and Wiley-Intersciece; Taub et al., J. Clin. Invest. 95:1370-1376, 1995; Lind et al., APMIS 103:140-146, 1995; Muller et al., Eur. J. Immunol. 25:1744-1748; Gruber et al., J. Immunol. 152:5860-5867, 1994; Johnston et al., J Immunol. 153:1762-1768, 1994.

Those proteins which exhibit activity as reproductive hormones or regulators of cell movement may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of reproductive hormones are beneficial. For example, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also exhibit activinor inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of FSH. Thus, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention, alone or in heterodimers with a member of the inhibin a family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin-B group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885, the disclosure of which is incorporated herein by reference. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

Alternatively, as described in more detail below, genes encoding reproductive hormone regulating activity proteins or nucleic acids regulating the expression of such

10

15

20

25

30

proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 37**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Chemotactic/Chemokinetic Activity

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for chemotactic/chemokinetic activity. For example, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: *Current Protocols in Immunology*, Ed by Coligan, Kruisbeek, Margulies, Shevach and Strober, Pub. Greene Publishing Associates and Wiley-

Interscience, Chapter 6.12: 6.12.1-6.12.28; Taub et al., J. Clin. Invest. 95:1370-1376, 1995; Lind et al., APMIS 103:140-146, 1995; Mueller et al., Eur. J. Immunol. 25:1744-1748; Gruber et al., J. Immunol. 152:5860-5867, 1994; Johnston et al. J. Immunol., 153:1762-1768, 1994.

5

10

15

20

25

### **EXAMPLE 38**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Blood Clotting

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effects on blood clotting. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79, 1991; Schaub, Prostaglandins 35:467-474, 1988.

Those proteins which are involved in the regulation of blood clotting may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of blood clotting is beneficial. For example, a protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulations disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as infarction of cardiac and central nervous system vessels (e.g., stroke)). Alternatively, as described in more detail below, genes encoding blood clotting activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 39**

30

Assaying the Proteins Expressed from Extended cDNAs or

Portions Thereof for Involvement in Receptor/Ligand Interactions

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for their involvement in receptor/ligand interactions. Numerous assays for such involvement are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Chapter 7. 7.28.1-7.28.22 in Current Protocols in Immunology, Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience; Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160, 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995; Gyuris et al., Cell 75:791-803, 1993.

For example, the proteins encoded by extended cDNAs derived from the 5' ESTs of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions. Alternatively, as described in more detail below, genes encoding proteins involved in receptor/ligand interactions or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

25

30

20

10

15

#### **EXAMPLE 40**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Anti-Inflammatory Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or

promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions, including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome), ischemia-reperfusioninury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine- or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material. Alternatively, as described in more detail below, genes encoding anti-inflammatory activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

15

20

25

30

10

. 5

#### **EXAMPLE 41**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Tumor Inhibition Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for tumor inhibition activity. In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth. Alternatively, as described in more detail below, genes tumor inhibition activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

10

15

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein. Alternatively, as described in more detail below, genes encoding proteins involved in any of the above mentioned activities or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

25

30

20

#### **EXAMPLE 42**

## Identification of Proteins which Interact with Polypeptides Encoded by Extended cDNAs

Proteins which interact with the polypeptides encoded by cDNAs derived from the 5' ESTs or fragments thereof, such as receptor proteins, may be identified using two hybrid systems such as the Matchmaker Two Hybrid System 2 (Catalog No. K1604-1, Clontech). As described in the manual accompanying the kit which is incorporated herein by reference,

10

15

20

25

30

the the cDNAs derived from 5' ESTs, or fragments thereof, are inserted into an expression vector such that they are in frame with DNA encoding the DNA binding domain of the yeast transcriptional activator GALA. cDNAs in a cDNA library which encode proteins which might interact with the polypeptides encoded by the extended cDNAs or portions thereof are inserted into a second expression vector such that they are in frame with DNA encoding the activation domain of GALA. The two expression plasmids are transformed into yeast and the yeast are plated on selection medium which selects for expression of selectable markers on each of the expression vectors as well as GALA dependent expression of the HIS3 gene. Transformants capable of growing on medium lacking histidine are screened for GALA dependent lacZ expression. Those cells which are positive in both the histidine selection and the lacZ assay contain plasmids encoding proteins which interact with the polypeptide encoded by the extended cDNAs or portions thereof.

Alternatively, the system described in Lustig et al., Methods in Enzymology 283: 83-99, 1997, and in U.S. Patent No. 5,654,150, the disclosure of which is incorporated herein by reference, may be used for identifying molecules which interact with the polypeptides encoded by extended cDNAs. In such systems, in vitro transcription reactions are performed on a pool of vectors containing extended cDNA inserts cloned downstream of a promoter which drives in vitro transcription. The resulting pools of mRNAs are introduced into Xenopus laevis oocytes. The oocytes are then assayed for a desired activity.

Alternatively, the pooled *in vitro* transcription products produced as described above may be translated *in vitro*. The pooled *in vitro* translation products can be assayed for a desired activity or for interaction with a known polypeptide.

Proteins or other molecules interacting with polypeptides encoded by extended cDNAs can be found by a variety of additional techniques. In one method, affinity columns containing the polypeptide encoded by the extended cDNA or a portion thereof can be constructed. In some versions, of this method the affinity column contains chimeric proteins in which the protein encoded by the extended cDNA or a portion thereof is fused to glutathione S-transferase. A mixture of cellular proteins or pool of expressed proteins as described above and is applied to the affinity column. Proteins interacting with the polypeptide attached to the column can then be isolated and analyzed on 2-D electrophoresis gel as described in Ramunsen et al., Electrophoresis 18:588-598,

10

15

20

25

30

species.

1997, the disclosure of which is incorporated herein by reference. Alternatively, the proteins retained on the affinity column can be purified by electrophoresis based methods and sequenced. The same method can be used to isolate antibodies, to screen phage display products, or to screen phage display human antibodies.

Proteins interacting with polypeptides encoded by extended cDNAs or portions thereof can also be screened by using an Optical Biosensor as described in Edwards and Leatherbarrow, Analytical Biochemistry 246:1-6, 1997, the disclosure of which is incorporated herein by reference. The main advantage of the method is that it allows the determination of the association rate between the protein and other interacting molecules. Thus, it is possible to specifically select interacting molecules with a high or low association rate. Typically a target molecule is linked to the sensor surface (through a carboxymethl dextran matrix) and a sample of test molecules is placed in contact with the target molecules. The binding of a test molecule to the target molecule causes a change in the refractive index and/ or thickness. This change is detected by the Biosensor provided it occurs in the evanescent field (which extend a few hundred nanometers from the sensor surface). In these screening assays, the target molecule can be one of the polypeptides encoded by extended cDNAs or a portion thereof and the test sample can be a collection of proteins extracted from tissues or cells, a pool of expressed proteins, combinatorial peptide and/ or chemical libraries, or phage displayed peptides. The tissues or cells from which the test proteins are extracted can originate from any

In other methods, a target protein is immobilized and the test population is a collection of unique polypeptides encoded by the extended cDNAs or portions thereof.

To study the interaction of the proteins encoded by the extended cDNAs or portions thereof with drugs, the microdialysis coupled to HPLC method described by Wang et al., Chromatographia 44:205-208, 1997 or the affinity capillary electrophoresis method described by Busch et al., J. Chromatogr. 777:311-328, 1997, the disclosures of which are incorporated herein by reference can be used.

It will be appreciated by those skilled in the art that the proteins expressed from the extended cDNAs or portions may be assayed for numerous activities in addition to those

10

15

specifically enumerated above. For example, the expressed proteins may be evaluated for applications involving control and regulation of inflammation, tumor proliferation or metastasis, infection, or other clinical conditions. In addition, the proteins expressed from the extended cDNAs or portions thereof may be useful as nutritional agents or cosmetic agents.

The proteins expressed from the cDNAs or portions thereof may be used to generate antibodies capable of specifically binding to the expressed protein or fragments thereof as described in Example 40 below. The antibodies may capable of binding a full length protein encoded by a cDNA derived from a 5' EST, a mature protein (i.e. the protein generated by cleavage of the signal peptide) encoded by a cDNA derived from a 5' EST, or a signal peptide encoded by a cDNA derived from a 5' EST. Alternatively, the antibodies may be capable of binding fragments of at least 10 amino acids of the proteins encoded by the above cDNAs. In some embodiments, the antibodies may be capable of binding fragments of at least 15 amino acids of the proteins encoded by the above cDNAs. In other embodiments, the antibodies may be capable of binding fragments of at least 25 amino acids of the proteins expressed from the extended cDNAs which comprise at least 25 amino acids of the proteins encoded by the above cDNAs. In further embodiments, the antibodies may be capable of binding fragments of at least 40 amino acids of the proteins encoded by the above cDNAs.

#### **EXAMPLE 43**

20

25

30

#### Production of an Antibody to a Human Protein

Substantially pure protein or polypeptide is isolated from the transfected or transformed cells as described in Example 30. The concentration of protein in the final preparation is adjusted, for example, by concentration on an Amicon filter device, to the level of a few µg/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows:

### 1. Monoclonal Antibody Production by Hybridoma Fusion

Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, and Milstein, *Nature* 256:495, 1975 or derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or

peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as ELISA, as originally described by Engvall, Meth. Enzymol. 70:419, 1980, the disclosure of which is incorporated herein by reference and derivative methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis et al. in Basic Methods in Molecular Biology Elsevier, New York. Section 21-2, the disclosure of which is incorporated herein by reference.

. 15

20

25

30

10

5

#### 2. Polyclonal Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogenous epitopes of a single protein can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than others and may require the use of carriers and adjuvant. Also, host animals response vary depending on site of inoculations and doses, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis. et al, J. Clin. Endocrinol. Metab. 33:988-991 (1971), the disclosure of which is incorporated herein by reference.

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, et al., Chap. 19 in: Handbook of Experimental Immunology D. Wier

10

15

20

25

30

(ed) Blackwell (1973), the disclosure of which is incorporated herein by reference. Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12 μM). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: *Manual of Clinical Immunology*, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D.C. (1980), the disclosure of which is incorporated herein by reference..

Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

## V. Use of 5' ESTs or Sequences Obtainable Therefrom or Portions Thereof as Reagents

The 5' ESTs of the present invention (or cDNAs or genomic DNAs obtainable therefrom) may be used as reagents in isolation procedures, diagnostic assays, and forensic procedures. For example, sequences from the 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) may be detectably labeled and used as probes to isolate other sequences capable of hybridizing to them. In addition, sequences from 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) may be used to design PCR primers to be used in isolation, diagnostic, or forensic procedures.

1. Use of 5' ESTs or Sequences Obtainable Therefrom or Portions Thereof in Isolation,

Diagnostic and Forensic Procedures

#### **EXAMPLE 44**

### Preparation of PCR Primers and Amplification of DNA

The 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom) may be used to prepare PCR primers for a variety of applications, including isolation procedures for cloning nucleic acids capable of hybridizing to such sequences, diagnostic techniques and

10

15

20

25

30

forensic techniques. The PCR primers are at least 10 bases, and preferably at least 12, 15, or 17 bases in length. More preferably, the PCR primers are at least 20-30 bases in length. In some embodiments, the PCR primers may be more than 30 bases in length. It is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see Molecular Cloning to Genetic Engineering, White Ed. in Methods in Molecular Biology 67: Humana Press, Totowa 1997, the disclosure of which is incorporated herein by reference. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid sample along with dNTPs and a thermostable polymerase such as Taq polymerase. Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites.

#### **EXAMPLE 45**

#### Use of 5'ESTs as Probes

Probes derived from 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom), including full length cDNAs or genomic sequences, may be labeled with detectable labels familiar to those skilled in the art, including radioisotopes and non-radioactive labels, to provide a detectable probe. The detectable probe may be single stranded or double stranded and may be made using techniques known in the art, including *in vitro* transcription, nick translation, or kinase reactions. A nucleic acid sample containing a sequence capable of hybridizing to the labeled probe is contacted with the labeled probe. If the nucleic acid in the sample is double stranded, it may be denatured prior to contacting the probe. In some applications, the nucleic acid sample may be immobilized on a surface such as a nitrocellulose or nylon membrane. The nucleic acid sample may comprise nucleic acids obtained from a variety of sources, including genomic DNA, cDNA libraries, RNA, or tissue samples.

Procedures used to detect the presence of nucleic acids capable of hybridizing to the detectable probe include well known techniques such as Southern blotting, Northern blotting,

10

15

20

dot blotting, colony hybridization, and plaque hybridization. In some applications, the nucleic acid capable of hybridizing to the labeled probe may be cloned into vectors such as expression vectors, sequencing vectors, or *in vitro* transcription vectors to facilitate the characterization and expression of the hybridizing nucleic acids in the sample. For example, such techniques may be used to isolate and clone sequences in a genomic library or cDNA library which are capable of hybridizing to the detectable probe as described in Example 30 above.

PCR primers made as described in Example 44 above may be used in forensic analyses, such as the DNA fingerprinting techniques described in Examples 46-50 below. Such analyses may utilize detectable probes or primers based on the sequences of the the 5' ESTs or of cDNAs or genomic DNAs isolated using the 5' ESTs.

#### **EXAMPLE 46**

### Forensic Matching by DNA Sequencing

In one exemplary method, DNA samples are isolated from forensic specimens of, for example, hair, semen, blood or skin cells by conventional methods. A panel of PCR primers based on a number of the 5' ESTs of Example 25, or cDNAs or genomic DNAs isolated therefrom as described above, is then utilized in accordance with Example 44 to amplify DNA of approximately 100-200 bases in length from the forensic specimen. Corresponding sequences are obtained from a test subject. Each of these identification DNAs is then sequenced using standard techniques, and a simple database comparison determines the differences, if any, between the sequences from the subject and those from the sample. Statistically significant differences between the suspect's DNA sequences and those from the sample conclusively prove a lack of identity. This lack of identity can be proven, for example, with only one sequence. Identity, on the other hand, should be demonstrated with a large number of sequences, all matching. Preferably, a minimum of 50 statistically identical sequences of 100 bases in length are used to prove identity between the suspect and the sample.

25

#### **EXAMPLE 47**

### Positive Identification by DNA Sequencing

The technique outlined in the previous example may also be used on a larger scale to provide a unique fingerprint-type identification of any individual. In this technique, primers are prepared from a large number of 5'EST sequences from Example 25, or cDNA or genomic DNA sequences obtainable therefrom. Preferably, 20 to 50 different primers are used. These primers are used to obtain a corresponding number of PCR-generated DNA segments from the individual in question in accordance with Example 44. Each of these DNA segments is sequenced, using the methods set forth in Example 46. The database of sequences generated through this procedure uniquely identifies the individual from whom the sequences were obtained. The same panel of primers may then be used at any later time to absolutely correlate tissue or other biological specimen with that individual.

#### **EXAMPLE 48**

#### 15

20

25

30

10

5

#### Southern Blot Forensic Identification

The procedure of Example 47 is repeated to obtain a panel of at least 10 amplified sequences from an individual and a specimen. Preferably, the panel contains at least 50 amplified sequences. More preferably, the panel contains 100 amplified sequences. In some embodiments, the panel contains 200 amplified sequences. This PCR-generated DNA is then digested with one or a combination of, preferably, four base specific restriction enzymes. Such enzymes are commercially available and known to those of skill in the art. After digestion, the resultant gene fragments are size separated in multiple duplicate wells on an agarose gel and transferred to nitrocellulose using Southern blotting techniques well known to those with skill in the art. For a review of Southern blotting see Davis et al. (Basic Methods in Molecular Biology, 1986, Elsevier Press. pp 62-65), the disclosure of which is incorporated herein by reference.

A panel of probes based on the sequences of 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom), or fragments thereof of at least 10 bases, are radioactively or colorimetrically labeled using methods known in the art, such as nick translation or end labeling, and hybridized to the Southern blot using techniques known in the art (Davis et al., supra). Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from

the 5' EST (or cDNAs or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the 5' EST (or cDNAs or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST (or cDNAs or genomic DNAs obtainable therefrom).

Preferably, at least 5 to 10 of these labeled probes are used, and more preferably at least about 20 or 30 are used to provide a unique pattern. The resultant bands appearing from the hybridization of a large sample of 5' EST (or cDNAs or genomic DNAs obtainable therefrom) will be a unique identifier. Since the restriction enzyme cleavage will be different for every individual, the band pattern on the Southern blot will also be unique. Increasing the number of 5' EST (or cDNAs or genomic DNAs obtainable therefrom) probes will provide a statistically higher level of confidence in the identification since there will be an increased number of sets of bands used for identification.

#### **EXAMPLE 49**

#### 15

20

25

30

10

5

#### **Dot Blot Identification Procedure**

Another technique for identifying individuals using the 5' EST sequences disclosed herein utilizes a dot blot hybridization technique.

Genomic DNA is isolated from nuclei of subject to be identified. Oligonucleotide probes of approximately 30 bp in length are synthesized that correspond to at least 10, preferably 50 sequences from the 5' ESTs or cDNAs or genomic DNAs obtainable therefrom. The probes are used to hybridize to the genomic DNA through conditions known to those in the art. The oligonucleotides are end labeled with P<sup>32</sup> using polynucleotide kinase (Pharmacia). Dot Blots are created by spotting the genomic DNA onto nitrocellulose or the like using a vacuum dot blot manifold (BioRad, Richmond California). The nitrocellulose filter containing the genomic sequences is baked or UV linked to the filter, prehybridized and hybridized with labeled probe using techniques known in the art (Davis et al., supra). The <sup>32</sup>P labeled DNA fragments are sequentially hybridized with successively stringent conditions to detect minimal differences between the 30 bp sequence and the DNA. Tetramethylammonium chloride is useful for identifying clones containing small numbers of nucleotide mismatches (Wood et al., Proc. Natl. Acad. Sci. USA 82(6):1585-1588, 1985)

which is hereby incorporated by reference. A unique pattern of dots distinguishes one individual from another individual.

5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom) or oligonucleotides containing at least 10 consecutive bases from these sequences can be used as probes in the following alternative fingerprinting technique. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom).

Preferably, a plurality of probes having sequences from different genes are used in the alternative fingerprinting technique. Example 50 below provides a representative alternative fingerprinting procedure in which the probes are derived from 5'EST.

#### 15

20

25

30

10

5

#### **EXAMPLE 50**

## Alternative "Fingerprint" Identification Technique

20-mer oligonucleotides are prepared from a large number, e.g. 50, 100, or 200, of 5'EST using commercially available oligonucleotide services such as Genset, Paris, France. Cell samples from the test subject are processed for DNA using techniques well known to those with skill in the art. The nucleic acid is digested with restriction enzymes such as EcoRI and XbaI. Following digestion, samples are applied to wells for electrophoresis. The procedure, as known in the art, may be modified to accommodate polyacrylamide electrophoresis, however in this example, samples containing 5 ug of DNA are loaded into wells and separated on 0.8% agarose gels. The gels are transferred onto nitrocellulose using standard Southern blotting techniques.

10 ng of each of the oligonucleotides are pooled and end-labeled with <sup>32</sup>P. The nitrocellulose is prehybridized with blocking solution and hybridized with the labeled probes. Following hybridization and washing, the nitrocellulose filter is exposed to X-Omat AR X-ray film. The resulting hybridization pattern will be unique for each individual.

It is additionally contemplated within this example that the number of probe sequences used can be varied for additional accuracy or clarity.

The proteins encoded by the extended cDNAs may also be used to generate antibodies as explained in Examples 30 and 43 in order to identify the tissue type or cell species from which a sample is derived as described in example 51.

5

10

15

20

25

30

#### **EXAMPLE 51**

# Identification of Tissue Types or Cell Species by Means of Labeled Tissue Specific Antibodies

Identification of specific tissues is accomplished by the visualization of tissue specific antigens by means of antibody preparations according to Examples 30 and 43 which are conjugated, directly or indirectly to a detectable marker. Selected labeled antibody species bind to their specific antigen binding partner in tissue sections, cell suspensions, or in extracts of soluble proteins from a tissue sample to provide a pattern for qualitative or semi-qualitative interpretation.

Antisera for these procedures must have a potency exceeding that of the native preparation, and for that reason, antibodies are concentrated to a mg/ml level by isolation of the gamma globulin fraction, for example, by ion-exchange chromatography or by ammonium sulfate fractionation. Also, to provide the most specific antisera, unwanted antibodies, for example to common proteins, must be removed from the gamma globulin fraction, for example by means of insoluble immunoabsorbents, before the antibodies are labeled with the marker. Either monoclonal or heterologous antisera is suitable for either procedure.

#### A. Immunohistochemical techniques

Purified, high-titer antibodies, prepared as described above, are conjugated to a detectable marker, as described, for example, by Fudenberg, Chap. 26 in: Basic and Clinical Immunology, 3rd Ed. Lange, Los Altos, California, 1980, or Rose, et al., Chap. 12 in: Methods in Immunodiagnosis, 2d Ed. John Wiley and Sons, New York (1980), the disclosures of which are incorporated herein by reference.

A fluorescent marker, either fluorescein or rhodamine, is preferred, but antibodies can also be labeled with an enzyme that supports a color producing reaction with a substrate, such as horseradish peroxidase. Markers can be added to tissue-bound antibody in a second step, as described below. Alternatively, the specific antitissue antibodies can be labeled with ferritin

10

15

20

25

30

or other electron dense particles, and localization of the ferritin coupled antigen-antibody complexes achieved by means of an electron microscope. In yet another approach, the antibodies are radiolabeled, with, for example <sup>125</sup>I, and detected by overlaying the antibody treated preparation with photographic emulsion.

Preparations to carry out the procedures can comprise monoclonal or polyclonal antibodies to a single protein or peptide identified as specific to a tissue type, for example, brain tissue, or antibody preparations to several antigenically distinct tissue specific antigens can be used in panels, independently or in mixtures, as required.

Tissue sections and cell suspensions are prepared for immunohistochemical examination according to common histological techniques. Multiple cryostat sections (about 4 μm, unfixed) of the unknown tissue and known control, are mounted and each slide covered with different dilutions of the antibody preparation. Sections of known and unknown tissues should also be treated with preparations to provide a positive control, a negative control, for example, pre-immune sera, and a control for non-specific staining, for example, buffer.

Treated sections are incubated in a humid chamber for 30 min at room temperature, rinsed, then washed in buffer for 30-45 min. Excess fluid is blotted away, and the marker developed.

If the tissue specific antibody was not labeled in the first incubation, it can be labeled at this time in a second antibody-antibody reaction, for example, by adding fluorescein- or enzyme-conjugated antibody against the immunoglobulin class of the antiserum-producing species, for example, fluorescein labeled antibody to mouse IgG. Such labeled sera are commercially available.

The antigen found in the tissues by the above procedure can be quantified by measuring the intensity of color or fluorescence on the tissue section, and calibrating that signal using appropriate standards.

### B. Identification of tissue specific soluble proteins

The visualization of tissue specific proteins and identification of unknown tissues from that procedure is carried out using the labeled antibody reagents and detection strategy as described for immunohistochemistry; however the sample is prepared according to an

10

15

20

25

30

electrophoretic technique to distribute the proteins extracted from the tissue in an orderly array on the basis of molecular weight for detection.

A tissue sample is homogenized using a Virtis apparatus; cell suspensions are disrupted by Dounce homogenization or osmotic lysis, using detergents in either case as required to disrupt cell membranes, as is the practice in the art. Insoluble cell components such as nuclei, microsomes, and membrane fragments are removed by ultracentrifugation, and the soluble protein-containing fraction concentrated if necessary and reserved for analysis.

A sample of the soluble protein solution is resolved into individual protein species by conventional SDS polyacrylamide electrophoresis as described, for example, by Davis, et al., Section 19-2 in: Basic Methods in Molecular Biology, Leder ed., Elsevier, New York, 1986. the disclosure of which is incorporated herein by reference, using a range of amounts of polyacrylamide in a set of gels to resolve the entire molecular weight range of proteins to be detected in the sample. A size marker is run in parallel for purposes of estimating molecular weights of the constituent proteins. Sample size for analysis is a convenient volume of from 5 to 55 µl, and containing from about 1 to 100 µg protein. An aliquot of each of the resolved proteins is transferred by blotting to a nitrocellulose filter paper, a process that maintains the pattern of resolution. Multiple copies are prepared. The procedure, known as Western Blot Analysis, is well described in Davis, L. et al., supra Section 19-3. One set of nitrocellulose blots is stained with Coomassie blue dye to visualize the entire set of proteins for comparison with the antibody bound proteins. The remaining nitrocellulose filters are then incubated with a solution of one or more specific antisera to tissue specific proteins prepared as described in Examples 30 and 43. In this procedure, as in procedure A above, appropriate positive and negative sample and reagent controls are run.

In either procedure A or B, a detectable label can be attached to the primary tissue antigen-primary antibody complex according to various strategies and permutations thereof. In a straightforward approach, the primary specific antibody can be labeled; alternatively, the unlabeled complex can be bound by a labeled secondary anti-IgG antibody. In other approaches, either the primary or secondary antibody is conjugated to a biotin molecule, which can, in a subsequent step, bind an avidin conjugated marker. According to yet another strategy, enzyme labeled or radioactive protein A, which has the property of binding to any IgG, is bound in a final step to either the primary or secondary antibody.

The visualization of tissue specific antigen binding at levels above those seen in control tissues to one or more tissue specific antibodies, prepared from the gene sequences identified from extended cDNA sequences, can identify tissues of unknown origin, for example, forensic samples, or differentiated tumor tissue that has metastasized to foreign bodily sites.

In addition to their applications in forensics and identification, 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) may be mapped to their chromosomal locations. Example 52 below describes radiation hybrid (RH) mapping of human chromosomal regions using 5'ESTs. Example 53 below describes a representative procedure for mapping an 5' EST to its location on a human chromosome. Example 54 below describes mapping of 5' ESTs on metaphase chromosomes by Fluorescence In Situ Hybridization (FISH). Those skilled in the art will appreciate that the method of Examples 52-54 may also be used to map cDNAs or genomic DNAs obtainable from the 5' ESTs to their chromosomal locations.

15

20

25

30

10

5

## 2. Use of 5' ESTs or Sequences Obtainable Therefrom or Portions Thereof in Chromosome Mapping

#### **EXAMPLE 52**

### Radiation hybrid mapping of 5'ESTs to the human genome

Radiation hybrid (RH) mapping is a somatic cell genetic approach that can be used for high resolution mapping of the human genome. In this approach, cell lines containing one or more human chromosomes are lethally irradiated, breaking each chromosome into fragments whose size depends on the radiation dose. These fragments are rescued by fusion with cultured rodent cells, yielding subclones containing different portions of the human genome. This technique is described by Benham et al., Genomics 4:509-517, 1989; and Cox et al., Science 250:245-250, 1990, the entire contents of which are hereby incorporated by reference. The random and independent nature of the subclones permits efficient mapping of any human genome marker. Human DNA isolated from a panel of 80-100 cell lines provides a mapping reagent for ordering 5'EST. In this approach, the frequency of breakage between markers is used to measure distance, allowing construction of fine resolution maps as has

15

20

25

30

been done using conventional ESTs (Schuler et al., Science 274:540-546, 1996, hereby incorporated by reference).

RH mapping has been used to generate a high-resolution whole genome radiation hybrid map of human chromosome 17q22-q25.3 across the genes for growth hormone (GH) and thymidine kinase (TK) (Foster et al., Genomics 33:185-192, 1996), the region surrounding the Gorlin syndrome gene (Obermayr et al., Eur. J. Hum. Genet. 4:242-245, 1996), 60 loci covering the entire short arm of chromosome 12 (Raeymaekers et al., Genomics 29:170-178, 1995), the region of human chromosome 22 containing the neurofibromatosis type 2 locus (Frazer et al., Genomics 14:574-584, 1992) and 13 loci on the long arm of chromosome 5 (Warrington et al., Genomics 11:701-708, 1991).

#### **EXAMPLE 53**

#### Mapping of 5'ESTs to HumanChromosomes using PCR techniques

5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) may be assigned to human chromosomes using PCR based methodologies. In such approaches, oligonucleotide primer pairs are designed from the 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) to minimize the chance of amplifying through an intron. Preferably, the oligonucleotide primers are 18-23 bp in length and are designed for PCR amplification. The creation of PCR primers from known sequences is well known to those with skill in the art. For a review of PCR technology see Erlich in PCR Technology, Principles and Applications for DNA Amplification, Freeman and Co., New York, 1992, the disclosure of which is incorporated herein by reference.

The primers are used in polymerase chain reactions (PCR) to amplify templates from total human genomic DNA. PCR conditions are as follows: 60 ng of genomic DNA is used as a template for PCR with 80 ng of each oligonucleotide primer, 0.6 unit of Taq polymerase, and 1 µCu of a <sup>32</sup>P-labeled deoxycytidine triphosphate. The PCR is performed in a microplate thermocycler (Techne) under the following conditions: 30 cycles of 94°C, 1.4 min; 55°C, 2 min; and 72°C, 2 min; with a final extension at 72°C for 10 min. The amplified products are analyzed on a 6% polyacrylamide sequencing gel and visualized by autoradiography. If the length of the resulting PCR product is identical to the distance between the ends of the primer sequences in the extended cDNA from which the primers are

15

25

30

derived, then the PCR reaction is repeated with DNA templates from two panels of human-rodent somatic cell hybrids, BIOS PCRable DNA (BIOS Corporation) and NIGMS Human-Rodent Somatic Cell Hybrid Mapping Panel Number 1 (NIGMS, Camden, NJ).

PCR is used to screen a series of somatic cell hybrid cell lines containing defined sets of human chromosomes for the presence of a given 5' EST (or cDNA or genomic DNA obtainable therefrom). DNA is isolated from the somatic hybrids and used as starting templates for PCR\_reactions using the primer pairs from the 5' EST (or cDNA or genomic DNA obtainable therefrom). Only those somatic cell hybrids with chromosomes containing the human gene corresponding to the 5' EST (or cDNA or genomic DNA obtainable therefrom) will yield an amplified fragment. The 5' EST (or cDNA or genomic DNA obtainable therefrom) are assigned to a chromosome by analysis of the segregation pattern of PCR products from the somatic hybrid DNA templates. The single human chromosome present in all cell hybrids that give rise to an amplified fragment is the chromosome containing that 5'EST (or cDNA or genomic DNA obtainable therefrom). For a review of techniques and analysis of results from somatic cell gene mapping experiments, see Ledbetter et al., Genomics 6:475-481, 1990, the disclosure of which is incorporated herein by reference.

#### **EXAMPLE 54**

## Mapping of Extended 5' ESTs to Chromosomes Using Fluorescence In Situ

## 20 - <u>Hybridization</u>

Fluorescence in situ hybridization allows the 5'EST (or cDNA or genomic DNA obtainable therefrom) to be mapped to a particular location on a given chromosome. The chromosomes to be used for fluorescence in situ hybridization techniques may be obtained from a variety of sources including cell cultures, tissues, or whole blood.

In a preferred embodiment, chromosomal localization of an 5'EST (or cDNA or genomic DNA obtainable therefrom) is obtained by FISH as described by Cherif *et al.* (*Proc. Natl. Acad. Sci. U.S.A.*, 87:6639-6643, 1990), the disclosure of which is incorporated herein by reference. Metaphase chromosomes are prepared from phytohemagglutinin (PHA)-stimulated blood cell donors. PHA-stimulated lymphocytes from healthy males are cultured for 72 h in RPMI-1640 medium. For synchronization, methotrexate (10 µM) is added for 17 h, followed by addition of 5-bromodeoxyuridine (5-BrdU, 0.1 mM) for 6 h. Colcemid (1

10

15

20

µg/ml) is added for the last 15 min before harvesting the cells. Cells are collected, washed in RPMI, incubated with a hypotonic solution of KCl (75 mM) at 37°C for 15 min and fixed in three changes of methanol:acetic acid (3:1). The cell suspension is dropped onto a glass slide and air dried. The 5'EST (or cDNA or genomic DNA obtainable therefrom) is labeled with biotin-16 dUTP by nick translation according to the manufacturer's instructions (Bethesda Research Laboratories, Bethesda, MD), purified using a Sephadex G-50 column (Pharmacia, Upsala, Sweden) and precipitated. Just prior to hybridization, the DNA pellet is dissolved in hybridization buffer (50% formamide, 2 X SSC, 10% dextran sulfate, 1 mg/ml sonicated salmon sperm DNA, pH 7) and the probe is denatured at 70°C for 5-10 min.

Slides kept at -20°C are treated for 1 h at 37°C with RNase A (100 µg/ml), rinsed three times in 2 X SSC and dehydrated in an ethanol series. Chromosome preparations are denatured in 70% formamide, 2 X SSC for 2 min at 70°C, then dehydrated at 4°C. The slides are treated with proteinase K (10 µg/100 ml in 20 mM Tris-HCl, 2 mM CaCl<sub>2</sub>) at 37°C for 8 min and dehydrated. The hybridization mixture containing the probe is placed on the slide, covered with a coverslip, sealed with rubber cement and incubated overnight in a humid chamber at 37°C. After hybridization and post-hybridization washes, the biotinylated probe is detected by avidin-FITC and amplified with additional layers of biotinylated goat anti-avidin and avidin-FITC. For chromosomal localization, fluorescent R-bands are obtained as previously described (Cherif et al., supra.). The slides are observed under a LEICA fluorescence microscope (DMRXA). Chromosomes are counterstained with propidium iodide and the fluorescent signal of the probe appears as two symmetrical yellow-green spots on both chromatids of the fluorescent R-band chromosome (red). Thus, a particular 5'EST (or cDNA or genomic DNA obtainable therefrom) may be localized to a particular cytogenetic R-band on a given chromosome.

25

Once the 5'EST (or cDNA or genomic DNA obtainable therefrom) have been assigned to particular chromosomes using the techniques described in Examples 52-54 above, they may be utilized to construct a high resolution map of the chromosomes on which they are located or to identify the chromosomes in a sample.

10

15

20

#### **EXAMPLE 55**

### Use of 5'EST to Construct or Expand Chromosome Maps

Chromosome mapping involves assigning a given unique sequence to a particular chromosome as described above. Once the unique sequence has been mapped to a given chromosome, it is ordered relative to other unique sequences located on the same chromosome. One approach to chromosome mapping utilizes a series of yeast artificial chromosomes (YACs) bearing several thousand long inserts derived from the chromosomes of the organism from which the extended cDNAs (or genomic DNAs obtainable therefrom) are obtained. This approach is described in Nagaraja et al., Genome Research 7:210-222 1997, the disclosure of which is incorporated herein by reference. Briefly, in this approach each chromosome is broken into overlapping pieces which are inserted into the YAC vector. The YAC inserts are screened using PCR or other methods to determine whether they include the 5'EST (or cDNA or genomic DNA obtainable therefrom) whose position is to be determined. Once an insert has been found which includes the 5'EST (or cDNA or genomic DNA obtainable therefrom), the insert can be analyzed by PCR or other methods to determine whether the insert also contains other sequences known to be on the chromosome or in the region from which the 5'EST (or cDNA or genomic DNA obtainable therefrom) was derived. This process can be repeated for each insert in the YAC library to determine the location of each of the extended cDNAs (or genomic DNAs obtainable therefrom) relative to one another and to other known chromosomal markers. In this way, a high resolution map of the distribution of numerous unique markers along each of the organisms chromosomes may be obtained.

As described in Example 56 below extended cDNAs (or genomic DNAs obtainable therefrom) may also be used to identify genes associated with a particular phenotype, such as hereditary disease or drug response.

3. Use of 5'ESTs or Sequences Obtained Therefrom or Fragments Thereof in Gene Identification

25

15

20

25

30

#### **EXAMPLE 56**

### Identification of genes associated with hereditary diseases or drug response

This example illustrates an approach useful for the association of 5'ESTs (or cDNA or genomic DNA obtainable therefrom) with particular phenotypic characteristics. In this example, a particular 5'EST (or cDNA or genomic DNA obtainable therefrom) is used as a test probe to associate that 5'EST (or cDNA or genomic DNA obtainable therefrom) with a particular phenotypic characteristic.

5'ESTs (or cDNA or genomic DNA obtainable therefrom) are mapped to a particular location on a human chromosome using techniques such as those described in Examples 52 and 53 or other techniques known in the art. A search of Mendelian Inheritance in Man (McKusick in *Mendelian Inheritance in Man* (available on line through Johns Hopkins University Welch Medical Library) reveals the region of the human chromosome which contains the 5'EST (or cDNA or genomic DNA obtainable therefrom) to be a very gene rich region containing several known genes and several diseases or phenotypes for which genes have not been identified. The gene corresponding to this 5'EST (or cDNA or genomic DNA obtainable therefrom) thus becomes an immediate candidate for each of these genetic diseases.

Cells from patients with these diseases or phenotypes are isolated and expanded in culture. PCR primers from the 5'EST (or cDNA or genomic DNA obtainable therefrom) are used to screen genomic DNA, mRNA or cDNA obtained from the patients. 5'ESTs (or cDNA or genomic DNA obtainable therefrom) that are not amplified in the patients can be positively associated with a particular disease by further analysis. Alternatively, the PCR analysis may yield fragments of different lengths when the samples are derived from an individual having the phenotype associated with the disease than when the sample is derived from a healthy individual, indicating that the gene containing the 5'EST may be responsible for the genetic disease.

## VI. Use of 5'EST (or cDNA or Genomic DNA Obtainable Therefrom) to Construct Vectors

The present 5'ESTs (or cDNA or genomic DNA obtainable therefrom) may also be used to construct secretion vectors capable of directing the secretion of the proteins

encoded by genes therein. Such secretion vectors may facilitate the purification or enrichment of the proteins encoded by genes inserted therein by reducing the number of background proteins from which the desired protein must be purified or enriched. Exemplary secretion vectors are described in Example 57 below.

**5** 

10

15

#### 1. Construction of Secretion Vectors

#### **EXAMPLE 57**

#### Construction of Secretion Vectors

The secretion vectors include a promoter capable of directing gene expression in the host cell, tissue, or organism of interest. Such promoters include the Rous Sarcoma Virus promoter, the SV40 promoter, the human cytomegalovirus promoter, and other promoters familiar to those skilled in the art.

A signal sequence from a 5' EST (or cDNAs or genomic DNAs obtainable therefrom) is operably linked to the promoter such that the mRNA transcribed from the promoter will direct the translation of the signal peptide. The host cell, tissue, or organism may be any cell, tissue, or organism which recognizes the signal peptide encoded by the signal sequence in the 5' EST (or cDNA or genomic DNA obtainable therefrom). Suitable hosts include mammalian cells, tissues or organisms, avian cells, tissues, or organisms, insect cells, tissues or organisms, or yeast.

20

In addition, the secretion vector contains cloning sites for inserting genes encoding the proteins which are to be secreted. The cloning sites facilitate the cloning of the insert gene in frame with the signal sequence such that a fusion protein in which the signal peptide is fused to the protein encoded by the inserted gene is expressed from the mRNA transcribed from the promoter. The signal peptide directs the extracellular secretion of the fusion protein.

25

30

The secretion vector may be DNA or RNA and may integrate into the chromosome of the host, be stably maintained as an extrachromosomal replicon in the host, be an artificial chromosome, or be transiently present in the host. Many nucleic acid backbones suitable for use as secretion vectors are known to those skilled in the art, including retroviral vectors, SV40 vectors, Bovine Papilloma Virus vectors, yeast integrating plasmids, yeast episomal plasmids, yeast artificial chromosomes, human artificial chromosomes, P element vectors,

10

15

20

baculovirus vectors, or bacterial plasmids capable of being transiently introduced into the host.

The secretion vector may also contain a polyA signal such that the polyA signal is located downstream of the gene inserted into the secretion vector.

After the gene encoding the protein for which secretion is desired is inserted into the secretion vector, the secretion vector is introduced into the host cell, tissue, or organism using calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection, viral particles or as naked DNA. The protein encoded by the inserted gene is then purified or enriched from the supernatant using conventional techniques such as ammonium sulfate precipitation, immunoprecipitation, immunochromatography, size exclusion chromatography, ion exchange chromatography, and HPLC. Alternatively, the secreted protein may be in a sufficiently enriched or pure state in the supernatant or growth media of the host to permit it to be used for its intended purpose without further enrichment.

The signal sequences may also be inserted into vectors designed for gene therapy. In such vectors, the signal sequence is operably linked to a promoter such that mRNA transcribed from the promoter encodes the signal peptide. A cloning site is located downstream of the signal sequence such that a gene encoding a protein whose secretion is desired may readily be inserted into the vector and fused to the signal sequence. The vector is introduced into an appropriate host cell. The protein expressed from the promoter is secreted extracellularly, thereby producing a therapeutic effect.

The 5' ESTs may also be used to clone sequences located upstream of the 5' ESTs which are capable of regulating gene expression, including promoter sequences, enhancer sequences, and other upstream sequences which influence transcription or translation levels. Once identified and cloned, these upstream regulatory sequences may be used in expression vectors designed to direct the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative fashion. Example 58 describes a method for cloning sequences upstream of the extended cDNAs or 5' ESTs.

25

10

15

20

25

30

## 2. Identification of Upstream Sequences With Promoting or Regulatory Activities EXAMPLE 58

#### Use of Extended cDNAs or 5' ESTs to Clone Upstream Sequences from Genomic DNA

Sequences derived from extended cDNAs or 5' ESTs may be used to isolate the promoters of the corresponding genes using chromosome walking techniques. In one chromosome walking technique, which utilizes the GenomeWalker<sup>TM</sup> kit available from Clontech, five complete genomic DNA samples are each digested with a different restriction enzyme which has a 6 base recognition site and leaves a blunt end. Following digestion, oligonucleotide adapters are ligated to each end of the resulting genomic DNA fragments.

For each of the five genomic DNA libraries, a first PCR reaction is performed according to the manufacturer's instructions (which are incorporated herein by reference) using an outer adaptor primer provided in the kit and an outer gene specific primer. The gene specific primer should be selected to be specific for the extended cDNA or 5' EST of interest and should have a melting temperature, length, and location in the extended cDNA or 5'EST which is consistent with its use in PCR reactions. Each first PCR reaction contains 5 ng of genomic DNA, 5 µl of 10X Tth reaction buffer, 0.2 mM of each dNTP, 0.2 µM each of outer adaptor primer and outer gene specific primer, 1.1 mM of Mg(OAc)<sub>2</sub>, and 1 µl of the Tth polymerase 50X mix in a total volume of 50 µl. The reaction cycle for the first PCR reaction is as follows: 1 min - 94°C / 2 sec - 94°C, 3 min - 72°C (7 cycles) / 2 sec - 94°C, 3 min - 67°C.

The product of the first PCR reaction is diluted and used as a template for a second PCR reaction according to the manufacturer's instructions using a pair of nested primers which are located internally on the amplicon resulting from the first PCR reaction. For example, 5 μl of the reaction product of the first PCR reaction mixture may be diluted 180 times. Reactions are made in a 50 μl volume having a composition identical to that of the first PCR reaction except the nested primers are used. The first nested primer is specific for the adaptor, and is provided with the GenomeWalker<sup>TM</sup> kit. The second nested primer is specific for the particular extended cDNA or 5' EST for which the promoter is to be cloned and should have a melting temperature, length, and location in the extended cDNA or 5' EST which is consistent with its use in PCR reactions. The reaction parameters of the second PCR reaction are as follows: 1 min -

10

15

20

25

30

94°C / 2 sec - 94°C, 3 min - 72°C (6 cycles) / 2 sec - 94°C, 3 min - 67°C (25 cycles) / 5 min - 67°C. The product of the second PCR reaction is purified, cloned, and sequenced using standard techniques.

Alternatively, two or more human genomic DNA libraries can be constructed by using two or more restriction enzymes. The digested genomic DNA is cloned into vectors which can be converted into single stranded, circular, or linear DNA. A biotinylated oligonucleotide comprising at least 15 nucleotides from the extended cDNA or 5' EST sequence is hybridized to the single stranded DNA. Hybrids between the biotinylated oligonucleotide and the single stranded DNA containing the extended cDNA or EST sequence are isolated as described in Example 29 above. Thereafter, the single stranded DNA containing the extended cDNA or EST sequence is released from the beads and converted into double stranded DNA using a primer specific for the extended cDNA or 5' EST sequence or a primer corresponding to a sequence included in the cloning vector. The resulting double stranded DNA is transformed into bacteria. DNAs containing the 5' EST or extended cDNA sequences are identified by colony PCR or colony hybridization.

Once the upstream genomic sequences have been cloned and sequenced as described above, prospective promoters and transcription start sites within the upstream sequences may be identified by comparing the sequences upstream of the extended cDNAs or 5' ESTs with databases containing known transcription start sites, transcription factor binding sites, or promoter sequences.

In addition, promoters in the upstream sequences may be identified using promoter reporter vectors as described in Example

#### **EXAMPLE 59**

### Identification of Promoters in Cloned Upstream Sequences

The genomic sequences upstream of the extended cDNAs or 5' ESTs are cloned into a suitable promoter reporter vector, such as the pSEAP-Basic, pSEAP-Enhancer, pßgal-Basic, pßgal-Enhancer, or pEGFP-1 Promoter Reporter vectors available from Clontech. Briefly, each of these promoter reporter vectors include multiple cloning sites positioned upstream of a reporter gene encoding a readily assayable protein such as secreted alkaline

10.

15

20

25

30

phosphatase,  $\beta$  galactosidase, or green fluorescent protein. The sequences upstream of the extended cDNAs or 5' ESTs are inserted into the cloning sites upstream of the reporter gene in both orientations and introduced into an appropriate host cell. The level of reporter protein is assayed and compared to the level obtained from a vector which lacks an insert in the cloning site. The presence of an elevated expression level in the vector containing the insert with respect to the control vector indicates the presence of a promoter in the insert. If necessary, the upstream sequences can be cloned into vectors which contain an enhancer for augmenting transcription levels from weak promoter sequences. A significant level of expression above that observed with the vector lacking an insert indicates that a promoter sequence is present in the inserted upstream sequence.

Appropriate host cells for the promoter reporter vectors may be chosen based on the results of the above described determination of expression patterns of the extended cDNAs and ESTs. For example, if the expression pattern analysis indicates that the mRNA corresponding to a particular extended cDNA or 5' EST is expressed in fibroblasts, the promoter reporter vector may be introduced into a human fibroblast cell line.

Promoter sequences within the upstream genomic DNA may be further defined by constructing nested deletions in the upstream DNA using conventional techniques such as Exonuclease III digestion. The resulting deletion fragments can be inserted into the promoter reporter vector to determine whether the deletion has reduced or obliterated promoter activity. In this way, the boundaries of the promoters may be defined. If desired, potential individual regulatory sites within the promoter may be identified using site directed mutagenesis or linker scanning to obliterate potential transcription factor binding sites within the promoter individually or in combination. The effects of these mutations on transcription levels may be determined by inserting the mutations into the cloning sites in the promoter reporter vectors.

#### **EXAMPLE 60**

#### Cloning and Identification of Promoters

Using the method described in Example 58 above with 5' ESTs, sequences upstream of several genes were obtained. Using the primer pairs GGG AAG ATG GAG ATA GTA TTG CCT G (SEQ ID NO:29) and CTG CCA TGT ACA TGA TAG AGA GAT TC (SEQ

10

15

20

25

30

ID NO:30), the promoter having the internal designation P13H2 (SEQ ID NO:31) was obtained.

Using the primer pairs GTA CCA GGGG ACT GTG ACC ATT GC (SEQ ID NO:32) and CTG TGA CCA TTG CTC CCA AGA GAG (SEQ ID NO:33), the promoter having the internal designation P15B4 (SEQ ID NO:34) was obtained.

Using the primer pairs CTG GGA TGG AAG GCA CGG TA (SEQ ID NO:35) and GAG ACC ACA CAG CTA GAC AA (SEQ ID NO:36), the promoter having the internal designation P29B6 (SEQ ID NO:37) was obtained.

Figure 4 provides a schematic description of the promoters isolated and the way they are assembled with the corresponding 5' tags. The upstream sequences were screened for the presence of motifs resembling transcription factor binding sites or known transcription start sites using the computer program MatInspector release 2.0, August 1996.

Table VII describes the transcription factor binding sites present in each of these promoters. The columns labeled matrice provides the name of the MatInspector matrix used. The column labeled position provides the 5' position of the promoter site. Numeration of the sequence starts from the transcription site as determined by matching the genomic sequence with the 5' EST sequence. The column labeled "orientation" indicates the DNA strand on which the site is found, with the + strand being the coding strand as determined by matching the genomic sequence with the sequence of the 5' EST. The column labeled "score" provides the MatInspector score found for this site. The column labeled "length" provides the length of the site in nucleotides. The column labeled "sequence" provides the sequence of the site found.

Bacterial clones containing plasmids containing the promoter sequences described above described above are presently stored in the inventor's laboratories under the internal identification numbers provided above. The inserts may be recovered from the deposited materials by growing an aliquot of the appropriate bacterial clone in the appropriate medium. The plasmid DNA can then be isolated using plasmid isolation procedures familiar to those skilled in the art such as alkaline lysis minipreps or large scale alkaline lysis plasmid isolation procedures. If desired the plasmid DNA may be further enriched by centrifugation on a cesium chloride gradient, size exclusion chromatography, or anion exchange chromatography. The plasmid DNA obtained using these procedures may then be manipulated using standard

10

15

20

cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the EST insertion. The PCR product which corresponds to the 5' EST can then be manipulated using standard cloning techniques familiar to those skilled in the art.

The promoters and other regulatory sequences located upstream of the extended cDNAs or 5' ESTs may be used to design expression vectors capable of directing the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative manner. A promoter capable of directing the desired spatial, temporal, developmental, and quantitative patterns may be selected using the results of the expression analysis described in Example 26 above. For example, if a promoter which confers a high level of expression in muscle is desired, the promoter sequence upstream of an extended cDNA or 5' EST derived from an mRNA which is expressed at a high level in muscle, as determined by the method of Example 26, may be used in the expression vector.

Preferably, the desired promoter is placed near multiple restriction sites to facilitate the cloning of the desired insert downstream of the promoter, such that the promoter is able to drive expression of the inserted gene. The promoter may be inserted in conventional nucleic acid backbones designed for extrachromosomal replication, integration into the host chromosomes or transient expression. Suitable backbones for the present expression vectors include retroviral backbones, backbones from eukaryotic episomes such as SV40 or Bovine Papilloma Virus, backbones from bacterial episomes, or artificial chromosomes.

Preferably, the expression vectors also include a polyA signal downstream of the multiple restriction sites for directing the polyadenylation of mRNA transcribed from the gene inserted into the expression vector.

Following the identification of promoter sequences using the procedures of Examples 58-60, proteins which interact with the promoter may be identified as described in Example 61 below.

25

15

20

25

30

#### EXAMPLE 61

## Identification of Proteins Which Interact with Promoter Sequences, Upstream Regulatory Sequences, or mRNA

Sequences within the promoter region which are likely to bind transcription factors may be identified by homology to known transcription factor binding sites or through conventional mutagenesis or deletion analyses of reporter plasmids containing the promoter sequence. For example, deletions may be made in a reporter plasmid containing the promoter sequence of interest operably linked to an assayable reporter gene. The reporter plasmids carrying various deletions within the promoter region are transfected into an appropriate host cell and the effects of the deletions on expression levels is assessed. Transcription factor binding sites within the regions in which deletions reduce expression levels may be further localized using site directed mutagenesis, linker scanning analysis, or other techniques familiar to those skilled in the art.

Nucleic acids encoding proteins which interact with sequences in the promoter may be identified using one-hybrid systems such as those described in the manual accompanying the Matchmaker One-Hybrid System kit available from Clontech (Catalog No. K1603-1), the disclosure of which is incorporated herein by reference. Briefly, the Matchmaker One-hybrid system is used as follows. The target sequence for which it is desired to identify binding proteins is cloned upstream of a selectable reporter gene and integrated into the yeast genome. Preferably, multiple copies of the target sequences are inserted into the reporter plasmid in tandem. A library comprised of fusions between cDNAs to be evaluated for the ability to bind to the promoter and the activation domain of a yeast transcription factor, such as GAL4, is transformed into the yeast strain containing the integrated reporter sequence. The yeast are plated on selective media to select cells expressing the selectable marker linked to the promoter sequence. The colonies which grow on the selective media contain genes encoding proteins which bind the target sequence. The inserts in the genes encoding the fusion proteins are further characterized by sequencing. In addition, the inserts may be inserted into expression vectors or in vitro transcription vectors. Binding of the polypeptides encoded by the inserts to the promoter DNA may be confirmed by techniques familiar to those skilled in the art, such as gel shift analysis or DNAse protection analysis.

## VII. Use of 5' ESTs (or cDNAs or Genomic DNAs Obtainable Therefrom) in Gene Therapy

The present invention also comprises the use of 5'ESTs (or cDNA or genomic DNA obtainable therefrom) in gene therapy strategies, including antisense and triple helix strategies as described in Examples 62 and 63 below. In antisense approaches, nucleic acid sequences complementary to an mRNA are hybridized to the mRNA intracellularly, thereby blocking the expression of the protein encoded by the mRNA. The antisense sequences may prevent gene expression through a variety of mechanisms. For example, the antisense sequences may inhibit the ability of ribosomes to translate the mRNA. Alternatively, the antisense sequences may block transport of the mRNA from the nucleus to the cytoplasm, thereby limiting the amount of mRNA available for translation. Another mechanism through which antisense sequences may inhibit gene expression is by interfering with mRNA splicing. In yet another strategy, the antisense nucleic acid may be incorporated in a ribozyme capable of specifically cleaving the target mRNA.

15

20

25

30

10

5

#### **EXAMPLE 62**

#### Preparation and Use of Antisense Oligonucleotides

The antisense nucleic acid molecules to be used in gene therapy may be either DNA or RNA sequences. They may comprise a sequence complementary to the sequence of the 5'EST (or cDNA or genomic DNA obtainable therefrom). The antisense nucleic acids should have a length and melting temperature sufficient to permit formation of an intracellular duplex with sufficient stability to inhibit the expression of the mRNA in the duplex. Strategies for designing antisense nucleic acids suitable for use in gene therapy are disclosed in Green et al., Ann. Rev. Biochem. 55:569-597, 1986; and Izant and Weintraub, Cell 36:1007-1015, 1984, which are hereby incorporated by reference.

In some strategies, antisense molecules are obtained from a nucleotide sequence encoding a protein by reversing the orientation of the coding region with respect to a promoter so as to transcribe the opposite strand from that which is normally transcribed in the cell. The antisense molecules may be transcribed using *in vitro* transcription systems such as those which employ T7 or SP6 polymerase to generate the transcript. Another approach

10

15

20

25

30

involves transcription of the antisense nucleic acids *in vivo* by operably linking DNA containing the antisense sequence to a promoter in an expression vector.

Alternatively, oligonucleotides which are complementary to the strand normally transcribed in the cell may be synthesized *in vitro*. Thus, the antisense nucleic acids are complementary to the corresponding mRNA and are capable of hybridizing to the mRNA to create a duplex. In some embodiments, the antisense sequences may contain modified sugar phosphate backbones to increase stability and make them less sensitive to RNase activity. Examples of modifications suitable for use in antisense strategies are described by Rossi *et al.*, *Pharmacol. Ther.* 50(2):245-254, 1991, which is hereby incorporated by reference.

Various types of antisense oligonucleotides complementary to the sequence of the 5'EST (or cDNA or genomic DNA obtainable therefrom) may be used. In one preferred embodiment, stable and semi-stable antisense oligonucleotides described in International Application No. PCT WO94/23026, hereby incorporated by reference, are used. In these molecules, the 3' end or both the 3' and 5' ends are engaged in intramolecular hydrogen bonding between complementary base pairs. These molecules are better able to withstand exonuclease attacks and exhibit increased stability compared to conventional antisense oligonucleotides.

In another preferred embodiment, the antisense oligodeoxynucleotides against herpes simplex virus types 1 and 2 described in International Application No. WO 95/04141, hereby incorporated by reference, are used.

In yet another preferred embodiment, the covalently cross-linked antisense oligonucleotides described in International Application No. WO 96/31523, hereby incorporated by reference, are used. These double- or single-stranded oligonucleotides comprise one or more, respectively, inter- or intra-oligonucleotide covalent cross-linkages, wherein the linkage consists of an amide bond between a primary amine group of one strand and a carboxyl group of the other strand or of the same strand, respectively, the primary amine group being directly substituted in the 2' position of the strand nucleotide monosaccharide ring, and the carboxyl group being carried by an aliphatic spacer group substituted on a nucleotide or nucleotide analog of the other strand or the same strand, respectively.

10

15

20

25

30

The antisense oligodeoxynucleotides and oligonucleotides disclosed in International Application No. WO 92/18522, incorporated by reference, may also be used. These molecules are stable to degradation and contain at least one transcription control recognition sequence which binds to control proteins and are effective as decoys therefore. These molecules may contain "hairpin" structures, "dumbbell" structures, "modified dumbbell" structures, "cross-linked" decoy structures and "loop" structures.

In another preferred embodiment, the cyclic double-stranded oligonucleotides described in European Patent Application No. 0 572 287 A2, hereby incorporated by reference are used. These ligated oligonucleotide "dumbbells" contain the binding site for a transcription factor and inhibit expression of the gene under control of the transcription factor by sequestering the factor.

Use of the closed antisense oligonucleotides disclosed in International Application No. WO 92/19732, hereby incorporated by reference, is also contemplated. Because these molecules have no free ends, they are more resistant to degradation by exonucleases than are conventional oligonucleotides. These oligonucleotides may be multifunctional, interacting with several regions which are not adjacent to the target mRNA.

The appropriate level of antisense nucleic acids required to inhibit gene expression may be determined using *in vitro* expression analysis. The antisense molecule may be introduced into the cells by diffusion, injection, infection, transfection or h-region-mediated import using procedures known in the art. For example, the antisense nucleic acids can be introduced into the body as a bare or naked oligonucleotide, oligonucleotide encapsulated in lipid, oligonucleotide sequence encapsidated by viral protein, or as an oligonucleotide operably linked to a promoter contained in an expression vector. The expression vector may be any of a variety of expression vectors known in the art, including retroviral or viral vectors, vectors capable of extrachromosomal replication, or integrating vectors. The vectors may be DNA or RNA.

The antisense molecules are introduced onto cell samples at a number of different concentrations preferably between  $1\times10^{-10}$ M to  $1\times10^{-10}$ M. Once the minimum concentration that can adequately control gene expression is identified, the optimized dose is translated into a dosage suitable for use *in vivo*. For example, an inhibiting concentration in culture of  $1\times10^{-7}$  translates into a dose of approximately 0.6 mg/kg bodyweight. Levels of oligonucleotide

10

15

20

approaching 100 mg/kg bodyweight or higher may be possible after testing the toxicity of the oligonucleotide in laboratory animals. It is additionally contemplated that cells from the vertebrate are removed, treated with the antisense oligonucleotide, and reintroduced into the vertebrate.

It is further contemplated that the antisense oligonucleotide sequence is incorporated into a ribozyme sequence to enable the antisense to specifically bind and cleave its target mRNA. For technical applications of ribozyme and antisense oligonucleotides see Rossi et al., supra.

In a preferred application of this invention, the polypeptide encoded by the gene is first identified, so that the effectiveness of antisense inhibition on translation can be monitored using techniques that include but are not limited to antibody-mediated tests such as RIAs and ELIŞA, functional assays, or radiolabeling.

The 5' ESTs of the present invention (or cDNAs or genomic DNAs obtainable therefrom) may also be used in gene therapy approaches based on intracellular triple helix formation. Triple helix oligonucleotides are used to inhibit transcription from a genome. They are particularly useful for studying alterations in cell activity as it is associated with a particular gene. The 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom) of the present invention or, more preferably, a portion of those sequences, can be used to inhibit gene expression in individuals having diseases associated with expression of a particular gene. Similarly, a portion of 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom) can be used to study the effect of inhibiting transcription of a particular gene within a cell. Traditionally, homopurine sequences were considered the most useful for triple helix strategies. However, homopyrimidine sequences can also inhibit gene expression. homopyrimidine oligonucleotides bind major groove homopurine:homopyrimidine sequences. Thus, both types of sequences from the 5'EST or from the gene corresponding to the 5'EST are contemplated within the scope of this invention.

25

10

15

20.

25

30

#### **EXAMPLE 63**

### Preparation and Use of Triple Helix Probes

The sequences of the 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) are scanned to identify 10-mer to 20-mer homopyrimidine or homopurine stretches which could be used in triple-helix based strategies for inhibiting gene expression. Following identification of candidate homopyrimidine or homopurine stretches, their efficiency in inhibiting gene expression is assessed by introducing varying amounts of oligonucleotides containing the candidate sequences into tissue culture cells which normally express the target gene. The oligonucleotides may be prepared on an oligonucleotide synthesizer or they may be purchased commercially from a company specializing in custom oligonucleotide synthesis, such as GENSET, Paris, France.

The oligonucleotides may be introduced into the cells using a variety of methods known to those skilled in the art, including but not limited to calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection or native uptake.

Treated cells are monitored for altered cell function or reduced gene expression using techniques such as Northern blotting, RNase protection assays, or PCR based strategies to monitor the transcription levels of the target gene in cells which have been treated with the oligonucleotide. The cell functions to be monitored are predicted based upon the homologies of the target gene corresponding to the extended cDNA from which the oligonucleotide was derived with known gene sequences that have been associated with a particular function. The cell functions can also be predicted based on the presence of abnormal physiologies within cells derived from individuals with a particular inherited disease, particularly when the extended cDNA is associated with the disease using techniques described in Example 56.

The oligonucleotides which are effective in inhibiting gene expression in tissue culture cells may then be introduced *in vivo* using the techniques described above and in Example 62 at a dosage calculated based on the *in vitro* results, as described in Example 62.

In some embodiments, the natural (beta) anomers of the oligonucleotide units can be replaced with alpha anomers to render the oligonucleotide more resistant to nucleases. Further, an intercalating agent such as ethidium bromide, or the like, can be attached to the 3' end of the alpha oligonucleotide to stabilize the triple helix. For information on the

10

15

20

25

generation of oligonucleotides suitable for triple helix formation see Griffin et al., Science 245:967-971, 1989, which is hereby incorporated by this reference.

#### **EXAMPLE 64**

# Use of cDNAs Obtained Using the 5' ESTs to Express an Encoded Protein in a Host Organism

The cDNAs obtained as described above using the 5' ESTs of the present invention may also be used to express an encoded protein in a host organism to produce a beneficial effect. In such procedures, the encoded protein may be transiently expressed in the host organism or stably expressed in the host organism. The encoded protein may have any of the activities described above. The encoded protein may be a protein which the host organism lacks or, alternatively, the encoded protein may augment the existing levels of the protein in the host organism.

A full length extended cDNA encoding the signal peptide and the mature protein, or an extended cDNA encoding only the mature protein is introduced into the host organism. The extended cDNA may be introduced into the host organism using a variety of techniques known to those of skill in the art. For example, the extended cDNA may be injected into the host organism as naked DNA such that the encoded protein is expressed in the host organism, thereby producing a beneficial effect.

Alternatively, the extended cDNA may be cloned into an expression vector downstream of a promoter which is active in the host organism. The expression vector may be any of the expression vectors designed for use in gene therapy, including viral or retroviral vectors. The expression vector may be directly introduced into the host organism such that the encoded protein is expressed in the host organism to produce a beneficial effect. In another approach, the expression vector may be introduced into cells *in vitro*. Cells containing the expression vector are thereafter selected and introduced into the host organism, where they express the encoded protein to produce a beneficial effect.

10

15

20

25

30

#### **EXAMPLE 65**

# Use of Signal Peptides Encoded by 5' ESTs or Sequences obtained Therefrom to Import Proteins Into Cells

The short core hydrophobic region (h) of signal peptides encoded by the 5'ESTS or extended cDNAs derived from SEQ ID NOs: 38-185 may also be used as a carrier to import a peptide or a protein of interest, so-called cargo, into tissue culture cells (Lin et al., J. Biol. Chem., 270: 14225-14258, 1995; Du et al., J. Peptide Res., 51: 235-243, 1998; Rojas et al., Nature Biotech., 16: 370-375, 1998).

When cell permeable peptides of limited size (approximately up to 25 amino acids) are to be translocated across cell membrane, chemical synthesis may be used in order to add the h region to either the C-terminus or the N-terminus to the cargo peptide of interest. Alternatively, when longer peptides or proteins are to be imported into cells, nucleic acids can be genetically engineered, using techniques familiar to those skilled in the art, in order to link the extended cDNA sequence encoding the h region to the 5' or the 3' end of a DNA sequence coding for a cargo polypeptide. Such genetically engineered nucleic acids are then translated either *in vitro* or *in vivo* after transfection into appropriate cells, using conventional techniques to produce the resulting cell permeable polypeptide. Suitable hosts cells are then simply incubated with the cell permeable polypeptide which is then translocated across the membrane.

This method may be applied to study diverse intracellular functions and cellular processes. For instance, it has been used to probe functionally relevant domains of intracellular proteins and to examine protein-protein interactions involved in signal transduction pathways (Lin et al., supra; Lin et al., J. Biol. Chem., 271: 5305-5308, 1996; Rojas et al., J. Biol. Chem., 271: 27456-27461, 1996; Liu et al., Proc. Natl. Acad. Sci. USA, 93: 11819-11824, 1996; Rojas et al., Bioch. Biophys. Res. Commun., 234: 675-680, 1997).

Such techniques may be used in cellular therapy to import proteins producing therapeutic effects. For instance, cells isolated from a patient may be treated with imported therapeutic proteins and then re-introduced into the host organism.

Alternatively, the h region of signal peptides of the present invention could be used in combination with a nuclear localization signal to deliver nucleic acids into cell nucleus. Such oligonucleotides may be antisense oligonucleotides or oligonucleotides designed to form

10

15

20

25

30

triple helixes, as described in examples 62 and 63 respectively, in order to inhibit processing and/or maturation of a target cellular RNA.

As discussed above, the cDNAs or portions thereof obtained using the 5' ESTs of the present invention can be used for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination for expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803, 1993, the disclosure of which is hereby incorporated by reference) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins or polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins

10

15

20

involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation *Molecular Cloning*; A Laboratory Manual, 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, Fritsch and Maniatis eds., 1989, and Methods in Enzymology; Guide to Molecular Cloning Techniques, Academic Press, Berger and Kimmel eds., 1987.

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Although this invention has been described in terms of certain preferred embodiments, other embodiments which will be apparent to those of ordinary skill in the art in view of the disclosure herein are also within the scope of this invention. Accordingly, the scope of the invention is intended to be defined only by reference to the appended claims. All documents cited herein are incorporated herein by reference in their entirety.

	Search characteristic	acteristic	Selection	Selection Characteristics	9
Sten	Program	Strand	Parameters	Identity (%)	Length (bp)
miscellanaeous	blastn	both	S=61 X=16	06	11
+RNA	fasta	both		80	09
rRNA	blastn	both	S=108	80	40
mtRNA	blastn	both	S=108	80	40
Procarvotic	blastn	both	S=144	06	40
Fungal	blastn	both	S=144	06	40
Alu	fasta*	both	•	70	40
	blastn	both	S=72	70	40
Repeats	blastn	both	S=72	70	40
Promoters	blastn	top	S=54 X=16	06	15†
Vertebrate	fasta*	both	S=108	90	30
ESTS	blastn	both	S=108 X=16	90	30
Proteins	blastx¤	top	E = 0.001	•	•

Table 1: Parameters used for each step of EST analysis

use "Quick Fast" Database scanner alignement further constrained to begin closer than 10bp to EST\u03b5' end using BLOSUM62 substitution matrix

TABLE II

SEQ. ID		<b>VON HELINE</b>	TISSUE	INTERNAL
<u>NO.</u>	CATEGORY	_SCORE_	SOURCE	DESIGNATION
		i i		
ID38	new	11.8	Umbilical cord	37-4-1-A12-PU
ID39	new .	10	Lymph ganglia	48-50-1-G11-PU
ID40	new	10	Lymph ganglia	48-16-2-C11-PU
ID41	new	10	Placenta	14-8-1-C10-PU
ID42	new	<b>9.9</b> .	Lymph ganglia	48-48-3-E11-PU
ID43	new	9.6	Lymph ganglia	48-26-2-B9-PU
ID44	new	9.2	Lymph ganglia	48-25-4-D9-PU
ID45	new	8.9	Lymph ganglia	48-67-2-F5-PU
ID46	new	8.9	Lymph ganglia	48-47-4-H7-PU
ID47	new	8.6	Lymph ganglia	48-52-1-E10-PU
ID48	new	8.5	Placenta	14-8-4-G8-PU
ID49	new _ ·	8.4	Lymph ganglia	48-4-2-G5-PU
ID50	new	8.2	Lymph ganglia	48-27-2-D7-PU
ID51	new	7	Lymph ganglia	48-61-3-F5-PU
ID52	new	6.9	Placenta	14-7-4-G8
ID53	new	6.9	Lymph ganglia	48-5-4-B6-PU
ID54	new	6.8	Lymph ganglia	48-46-3-C8-PU
ID55	new	6.7	Lymph ganglia	48-20-3-A6-PU
ID56	new	6.6	Lymph ganglia	48-18-2-F6-PU
ID57	new	6.5	Lymph ganglia	48-2-2-A10-PU
ID58	new	6.5	Lymph ganglia	48-25-4-C11-PU
ID59	new	6.3	Lymph ganglia	48-26-1-C4-PU
ID60	new	6.3	Lymph ganglia	48-31-2-G8-PU
ID61	new	6.3	Lymph ganglia	48-24-1-D8-PU
ID62	new	6.3	Umbilical cord	37-11-2-D10-PU
ID63	new	6.3	Lymph ganglia	48-8-2-C2-PU
ID64	new	6.2	Lymph ganglia	48-20-4-A8-PU
ID65	new	6.1	Lymph ganglia	48-2-1-B9-PU
ID66	new	6.1	Lymph ganglia	48-54-1-G9-PU
ID67	new	6.1	Lymph ganglia	48-47-4-B7-PU
ID68 -	new	6.1	Lymph ganglia	48-8-1-D8-PU
ID69	new	5.9	Lymph ganglia	48-12-3-G8-PU
ID70	new	5.9	Umbilical cord	37-39-4-A5-PU
ID71	new	5.9	Lymph ganglia	48-25-1-B6-PU
ID72	new	5.7	Lymph ganglia	48-15-1-D2-PU
ID73	new .	5.5	Umbilical cord	37-3-4-D1-PU
ID74	new	5.4	Lymph ganglia	48-13-1-G4-PU
ID75	new	5.4	Lymph ganglia	48-10-1-E4-PU
ID76	new	5.2	Lymph ganglia	48-8-1-A3-PU
ID77	new	5.2	Umbilical cord	37-7-4-F2-PU
ID78	new	5.2	Lymph ganglia	48-50-3-F1-PU
ID79	new	5.2	Lymph ganglia	48-8-2-B5-PU
ID80	new	5	Placenta	
ID81	new	5	•	11-4-0-B11-RP
ID82		4.9	Lymph ganglia	48-48-4-H11-PU
ID83	new	4.8	Umbilical cord	37-2-1-B4-PU
ID84	new		Lymph ganglia	48-47-2-B2-PU
ID85	new	4.8	Lymph ganglia	48-3-4-C11-PU
ID86	new	4.8	Lymphocytes	24-6-1-C8-PU
T) OO	new	4.8	Placenta	31-10-3-D2-PU

SEQ. ID		VON HEIJNE	TISSUE	INTERNAL
NO.	CATEGORY	_SCORE_	SOURCE	DESIGNATION
	•			
ID87	new	4.7	Lymph ganglia	48-54-3-F9-PU
ID88	new	4.7	Lymph ganglia	48-47-1-C9-PU
ID89	new	4.7	Lymph ganglia	48-4-2-C9-PU
ID90	new	4.6	Umbilical cord	37-33-2-E2-PU
ID91	new	4.5	Umbilical cord	37-2-1-B7-PU
ID92	new	4.5	Lymph ganglia	48-51-2-C3-PU
ID93	new	4.5	Lymph ganglia	48-23-4-D4-PU
ID94	new	4.4	Umbilical cord	37-4-1-A6-PU
ID95	new	4.4	Lymph ganglia	48-11-4-C10-PU
ID96	new	4.4	Umbilical cord	37-1-4-F3-PU
ID97	new	4.3	Lymphocytes	24-2-2-G10-PU
ID98	new	4.3	Lymph ganglia	48-26-3-G3-PU
ID99	new	4.1	Lymph ganglia	48-20-3-H2-PU
ID100	new	4.1	Lymph ganglia	48-31-3-F7-PU
ID101	new	4.1	Lymph ganglia	48-29-1-H9-PU
ID102	new	4.1	Umbilical cord	37-1-3-G4-PU
ID103	new	4.1	Umbilical cord	37-8-3-G12-PU
ID104	new	4.1	Lymph ganglia	48-26-4-G1-PU
ID105	new .	4	Lymph ganglia	48-27-1-B12-PU
ID106	new	4	Lymph ganglia	48-22-1-H7-PU
ID107	new	4	Lymphocytes	24-1-4-F9-PU
ID108	new	4	Lymph ganglia	48-6-2-A1-PU
ID109	new	4	Umbilical cord	37-3-3-B3-PU
ID110	new	3.8	Umbilical cord	37-7-2-F6-PU
ID111	new	3.8	Lymph ganglia	48-52-1-A6-PU
ID112	new	3.8	Lymph ganglia	48-7-2-F5-PU
ID113	new	3.8	Umbilical cord	37-12-2-D12-PU
ID114	new	3.8	Umbilical cord	37-11-3-D2-PU
ID115	new	3.8	Lymph ganglia	48-1-1-H7-PU
<b>D</b> 116	new	3.7	Lymph ganglia	48-21-3-E1-PU
ID117	new	3.6	Lymph ganglia	48-26-3-B8-PU
ID118	new	3.6	Umbilical cord	37-9-2-D9-PU
ID119 -	new	3.6	Lymph ganglia	48-3-3-A3-PU
ID120	new	3.6	Lymphocytes	24-1-3-G11-PU
ID121	new	3.6	Lymphocytes	24-4-1-A4-PU
ID122	new	3.5	Lymph ganglia	48-23-2-B12-PU
ID123	new	3.5	Lymph ganglia	48-47-3-F2-PU
ID124	new	3.5	Lymphocytes	24-4-4-H11-PU
ID125	new	3.5	Lymph ganglia	48-7-3-B8-PU
ID126	ext-est-not-vrt	12.8	Lymph ganglia	48-12-4-E3-PU
ID127	ext-est-not-vrt	9.3	Umbilical cord	37-12-3-G9-PU
ID128	ext-est-not-vrt	9.3	Lymph ganglia	48-67-4-A6-PU
ID129	ext-est-not-vrt	8.1	Lymph ganglia	48-28-3-A9-PU
ID130	ext-est-not-vrt	7.7	Lymphocytes	24-3-3-C6-PU
ID131	ext-est-not-vrt	6.6	Lymph ganglia	48-28-4-C2-PU
ID131	ext-est-not-vrt	6.2	Lymph ganglia	48-25-2-A1-PU
ID132	ext-est-not-vrt	5.8	Lymph ganglia	48-24-4-B7-PU
ID133		5.3		48-6-1-C9-PU
	ext-est-not-vrt	5.1	Lymph ganglia	
ID135	ext-est-not-vrt	3.1 4.6	Lymph ganglia	48-7-4-H2-PU
ID136	ext-est-not-vrt		Lymph ganglia	48-28-3-B6-PU
ID137	ext-est-not-vrt	4.4	Lymph ganglia	48-3-1-H9-PU

SEQ. ID	0.4	VON HELINE	TISSUE	INTERNAL
NO.	CATEGORY	SCORE	SOURCE	<u>DESIGNATION</u>
ID138	out act not set	4.4	77 1 *4* 1 · 1	
ID139	ext-est-not-vrt	4.4	Umbilical cord	37-6-4-B11-PU
ID139	ext-est-not-vrt	3.9	Lymph ganglia	48-26-1-G10-PU
ID140 ID141		3.8	Umbilical cord	37-9-4-H9-PU
	ext-est-not-vrt	3.7	Lymphocytes	24-1-4-F8-PU
ID142	ext-est-not-vrt	3.5	Lymph ganglia	48-21-3-H7-PU
ID143	est-not-ext	11.7	Lymph ganglia	48-6-4-G3-PU
ID144	est-not-ext	10.9	Umbilical cord	37-5-1-A12-PU
ID145	est-not-ext	10.9	Lymph ganglia	48-22-4-A8-PU
ID146	est-not-ext	9.6	Lymph ganglia	48-27-1-B8-PU
ID147	est-not-ext	9.6	Umbilical cord	37-4-1-G3-PU
ID148	est-not-ext	9.3	Lymph ganglia	48-11-4-E3-PU
ID149	est-not-ext	8.2	Lymph ganglia	48-25-4-D8-PU
ID150	est-not-ext	8.2	Lymph ganglia	48-19-3-G1-PU
D151		8.1	Placenta	31-11-4-B2-PU
ID152	est-not-ext	7.9	Lymph ganglia	48-7-4-H10-PU
ID153	est-not-ext	7.7	Lymph ganglia	48-11-4-F7-PU
ID154	est-not-ext	7.2	Lymph ganglia	48-10-3 <b>-</b> B5-PU
ID155	est-not-ext	6.9	Umbilical cord	37-8-4-D3-PU
ID156	est-not-ext	6.4	Umbilical cord	37-6-2-D10-PU
ID157	est-not-ext	6.3	Lymph ganglia	48-17-1-D11-PU
ID158	est-not-ext	6.1	Lymphocytes	24-8-3-G1-PU
ID159	est-not-ext	6.1	Umbilical cord	37-12-2-D1-PU
ID160	est-not-ext	6.1	Umbilical cord	37-6-2-A10-PU
ID161	est-not-ext	6	Lymph ganglia	48-26-1-A11-PU
ID162	est-not-ext	5.9	Lymph ganglia	48-60-4-H5-PU
ID163	est-not-ext	5.8	Umbilical cord	37-29-2-G3-PU
ID164	est-not-ext	5.7	Umbilical cord	37-28-2-D3-PU
ID165	est-not-ext	5.6	Lymph ganglia	48-49-1-F5-PU
ID166	est-not-ext	5,5	Umbilical cord	37-2-2-D12-PU
ID167	est-not-ext	5.5	Umbilical cord	37-7-4-B3-PU
ID168	est-not-ext	5,3	Lymph ganglia	48-24-1-D2-PU
<b>D</b> 169	est-not-ext	5	Lymph ganglia	48-21-4-H4-PU
ID170 -	est-not-ext	4.9	Umbilical cord	37-41-4-B9-PU
ID171	est-not-ext	4.9	Lymph ganglia	48-12-3-E2-PU
ID172	est-not-ext	4.6	Lymph ganglia	48-5-4-C5-PU
ID173	est-not-ext	4.3	Lymphocytes	24-5-1-E2-PU
ID174	est-not-ext	4.1	Lymph ganglia	48-18-3-F9-PU
ID175	est-not-ext	4.1	Lymphocytes	24-5-1-H2-PU
ID176	est-not-ext	3.8	Lymph ganglia	48-6-2-G1-PU
ID177	est-not-ext	3.8	Umbilical cord	37-9-2-G10-PU
ID178	est-not-ext	3.7	Lymph ganglia	48-19-3-A7-PU
ID179	est-not-ext	3.5	Lymph ganglia	48-13-3-E3-PU
ID180	est-not-ext	3.5	Lymph ganglia	48-20-4-G6-PU
ID181	est-not-ext	3.5	Lymphocytes	24-4-I-G11-PU
ID182	est-not-ext	3.5		_
ID182	ext-vrt-not-genomic	8.4	Lymph ganglia	48-4-2-E4-PU
ID183	ext-vrt-not-genomic		Lymph ganglia	48-24-1-B3-PU
ID185	ext-vrt-not-genomic	7.4 6.5	Lymph ganglia	48-30-2-B2-PU
101	CVI-ALI-HOL-ROHOHIG	0.5	Umbilical cord	37-30-2-B3-PU

### TABLE III

SEQ. ID	
_NO	SIGNAL PEPTIDE
	BIONALLE TIPL
ID38	MVLVALILHSALA
ID39	MAQHHLWILLCLQTWPEAAG
ID39 ID40	MKDLWIFLLLVTAPRCILS
ID41	MAQHILWILLCLQTWPEAAG
ID42	MDWTWRFLFVVAAATGVQS
ID43	MSICFLGLLLCLIPHRLA
ID44	MIGFLVLLILPLLSSLS
ID45	MQCLLSVLMAQFIXHFLSLLMSLLVSTVTWQ
ID46	MELGLSWIFFLATLKGVQC
ID47	MVSVSLALLSGWVGS
ID48	MPLPWSLALPLLLSWVAGGFG
ID49	MVSNFFHVIQVFEKSATLISKTEHIGFVIYSWXKSTTHLGSRRKFAISIYLSEVSLQKYD
•	CPFSGTSFVVFSLFLICAMA
ID50	MRXFWFLMYPFRFHDCKQKYDLYISIAGWLIICLACVLFPLLRT
ID51	MVSLCCLFTCFFIPCIS
ID52	MDFFFLERSYWGKMILLLVTYSPIAYS
ID53	MTMRHNWTPDLSPLWVLLLCAHVVTL
ID54	MDNMSGGKVDEALVKSSCLHPWSKRNDVSMQCSQDILRMLLSLQPVLQ
ID55	MXLQGQEATGKVLIKIHKDTSQVPTAXGDASIAALVLWTLPGAQR
ID56	MTEHSLTHQGIPILVLILFPTSCVM
ID57	MYIGGLRFIFLTSLOLISS
ID58	MSVSLKHIHLHFIIMSVLVFWNCSHLIFFSLIFLNLFA
ID59	MXXLGXXRFMVSFLSXPFLCSA
ID60	MDWTWYILVSVAAATGAHS
ID61	MISKFSSKAYSVRGLELFSLLPINPSPNSAIXVACVLSSLIAVNS
ID62	MVLLGAFGSCIKSFSLLFLIFSLNLNRG
ID63	MAARQAVGSGAQETCGLDRILEALKLLLSPGXSGS
ID64	MSTQKGLALFLMALGFSCI
ID65	MKDVEIIMIFHGYFLIVFFVFLCNC
ID66	MCFPEHRRQMYIQDRLDSVTRRARQGRICAILLLQSQCAYWA
ID67 -	MLVVKQCFSDSSILSTFVSWLSA
ID68	MIXLRDTAASLRLERDTRQLPLLTSALHGLQQ
ID69	MITMMLALISVCLF
ID70	MWLLTLVQCSDLCPS
ID71	MRVHLFPYLCQPSVLSNFLLFACLTMLLVKT
ID72	MIPLCFLILPYPVLS
ID73	MAGSRLPRQLFLQGVXASSCLLSXPSTRKSQA
ID74	MYICFCLESFEIKCGFVLHLLAQDLVCC
ID75	MHFILHNLNAFTLLVWLSLS
ID76	MSFFPFNRSLNSNPHPNLLFPNIAPLFTLLPKSIP
ID77	MVVWVLEVRFLLDLHCFCSLAKT
ID78	MVCGWWTQGPVPGLCCPALGSAWS
ID79	MGRAFPSRHKTARFECALVSASLTTA
ID80	MGLKALCXXLLCVLFVSH
ID81	MMATQTLSIDSYQDGQQMQVVTELKTEQDPNCSEPDAEGVSPPPVESQTPMDVDKQAIYR
,	HPLFPLLALLFEKCEQ
ID82	MSPSQLTCSVFLSGSVCLSFL
ID83	MLQALAPAHHLCSLKRSFCSLLCLRTQLFP
ID84	MLFLKYLWRSLCRG
	The state of the s

SEQ. ID	· .
NO.	SIĞNAL PEPTIDE
<del>-1:21-</del>	
ID85	MALLAMHSWRWAAAAAAFEKRRHSAILIRPLVSVSGS
ID86	
	MKAXAMFGAGDEDDTDFLSPSGGARLASLFGLDQXAAG
ID87	MLWLLRSLTDVSS
ID88	MTIFHVLIAHSSSFS
ID89	MHWQLLXGFCGSYSA
ID90	MTMMVMASFLPRNTMYTNTMNYSIFVFLLFFFSXLXY
ID91	MPSQTLSQPRISVLHGDLVPAGMAVQEIGAQMVLPCEVVSGSGLTREHLVTRLALCQS
	PRA
ID92	MSLRVHTLPTLLGAVVRPGCRELLCLLMITVTVGPGAS
ID93	MIYLTSLLLLGRWLTLTS
ID94	MNWNVRGTRGFLLCPLVCGLRR
ID95	MEQAALEVVSPLPRRCSVRSPVTTCCAKDLVCLTFITATTHE
ID96	MIIPLPSLVGCWEGGNGKGLMVSDTTCWTLASSNVPSPSPAPTLGRGAPSHTPQKKPTIP
	GARHRPIILPKGLVQLHATXLALG
ID97	MSMRLSGERIYLLLEVWLPXLNFESVLHFIQTVHIALPGSLG
ID98	MGTLLLFCFMPVVINP
ID99	MVVLNPMTLGIYLQLFFLSIVS
ID100	MAPHTASFGVCPLLSVTRVVATEHWLFLASLSGIKT
ID101	MSYKWMPSLPCLSFCTLCLV
ID102	MPLPTWAPTLAGFLLVLYVCLP
ID103	MNLYLLDWIGLKALIRG
ID104	MSCXVXDAXXRWWAHXLIIGWXHLTQKVHPIALSHCVNMGTLLLFCFMPVVINP
ID105	MVPNLCGRQILAFQTFLLNLRA
	· · · · · · · · · · · · · · · · · · ·
ID106	MFSLIIFFPPSSP
ID107	MSAFYLSYSLLHCLLIVFILVEF
ID108	MAEAKLVQGSLVAPQRXSAGVVLTMDGASA
ID109	MKGVGPEQLNDGAPSNEIEMTPCFFSEFLLLDVGVVNIVVIKMSYNVLLTISTNASVLG
ID110	MLRKLSASNENLCLLSNPSHNEVYLIRCCESHQLFWVTASTFCRS
ID111	MYPLILLPLNPFVLQ
ID112	MLLRPSPGSPRGFVAVGLGQISA
ID113	MARPGATACGPAAHQCSA
ID114	MEPVSSLSLCIXXLEHLFT
ID115 -	MRPAGRWCSAAAWRSPLSA
ID116	MWLCAYVLFFFNGCLY
D117	MLLLHRAVVLRLQQA
	MEMFGXXEKDFSSVEGVLXSLVPSMCFHVTNS
ID118	
ID119	MQMHGWRWDPHSSEQLDLAHTLSREASLENNTALLGVHASFQMSVA
ID120	MASPRGTDYNQTPNTTMYCYAVGTGVLTSRLARA
ID121	MAPILSSFKSLLKYHLLETSLSILLKPVTLHCLCPFPALFLS
ID122	MNRLSKHLIILVPWWLPPFVYT
ID123	MSSNKEQRSAVFVILFALITILILYSSNS
ID124	MDMKSNTGHGLFLGRQPSFSVRSMPGTPALAICQPHNPGPPMGTPTEDPSGCSFPCLFLS
	POSFLVLS
ID125	MSEAGCKPSRPEHGSFLSLSSTLLLTSHH
ID126	MESGXGXVFLVALLRGVQC
ID127	MLCRLFTLLLLQSLLLG
	· · · · · · · · · · · · · · · · · · ·
ID128	MOLLHKNMKHLWFFLLLVAGPRWVLS
ID129	MQAQAPVVVVTQPGVGPGPAPQNSNWQTGMCDCFSDCGVCLCGTFCFPCLG
ID130	MKALCLLLLPVLGLLVSS
ID131	MSPSGRLCLLXIVGLXLPTXG
ID132	MLLAWVQAFLVSNMLLAEAYG
-	

SEQ. ID	·
_NO	SIGNAL PEPTIDE
ID133	MLSESRGPPVQEHEAPVVLPPAGGGSQMGPVPAAXAGESGPGXVKPLETLXLTCSVSGGS
	IS
ID134	MTSGQARASXQSPQALEDSGPVNISVSITLTLDPLKPFGGYSRNVTHLYSTILGHQIGLS
	GREAHEEINITFTLPTAWSSDDCALHGHCEQVVFTACMTLTASPGVFP
ID135	MLGGDHRALLLKIWLLQRPES
ID136	MRFRKAWAPVLAALSHSLMSLLDESSCQA
ID137	MYVWPCAVVLAQYLWFHRRSLPGKAILEIGAGVSLPGILAAKCGAEVILSDSSELPHCLE
	VCRQSCQMINILPHLQVVGLTWG
ID138	MLNPAQXDTMPCEYLSLDAMEKWIIFGFILCHGILNTXATALNLWKLALQSSSCLS
ID139	MNAQASSSRCHGVCLSVPSLPSIS
ID140	MAKVQVNNVVVLDNPSPFYNPFQFEITFECIEDLSEDLEWKIIYVGSAESEEYDQVLDSV
	LVGPVPA
ID141	MADVEDGEETCALASHSGSSG
ID142	MWTCLLGDCGPPEA
ID143	MDWTWXVFCLLAVAPGAHS
ID144	MDNSWRLGPAIGLSAGQSQLLVSLLLLLTRVQP
ID145	MXHLXFFLLLVAAPRWVLS
ID146	MPVPASWPHPPGPFLLLTLLLGLTEVAG
ID147	MKEYVLLIFLALCSA
ID148	MAQSLALSLLILVLAFG
ID149	MKKVLLLITAILAVAVG
ID150	MKKVLLLITAILAVAVG
ID151	MRIMLLFTAILAFSLAQS
ID151	MAWTVLLLGLLSHCTVS
ID153	MTILHTGXNPFRPSQRWTAPALLHHRPXTXPPSXHRSRCTEXVGIPXLLLQTLPASTX
ID155 ID154	MKHLWFFLLLLVAAPKXXLS
ID155	MLSYFLSSLVCGSLGLSNVSG
ID156	MGTQDPQAEQGLRIPLPGLLLSKHHHPAPELPALALLHAGHA
ID150	MMTTYALSNEFAFKINEEQLSXXPLXSVQLXHA
ID158	MRGAHLXALEMLTAFASHIRA
ID150 ID159	MNPESPQQLERQSTGPRTGTRRCLSKFTWCTSRMMTOTCIILLIHTMOVCTT
ID160	MMTQTCILLIHTMQVCTT
ID161 -	MAGKGSSGRRPLLLGLLVAVATVHL
ID162	MAGSPTCLTLIYILWQLTGSAA
ID163	MVGMVCFIILGLIICIQC
ID164	MXLLHSLSSGVRA
ID165	MTMAECPTLCVSSSPALWA
ID166	
	MVPLVAVVSGPRAQLFACLLRLGTQ
ID167	MSEMAELSELYEESSDLQMDVMPGEGDLPQMEVGSGSRELSLRPSRSGAQQLEEEGPMEE
TD1/0	EEAQPMAXQRGNGALLTGPTLGSSQA
ID168	MLIVSVLALIPXTTT
ID169	MTCRGSCSYATRRSPSELSLLPSSLWVLA
ID170	MEAVVFVFSLLDCCA
D171	MAATSGTDEPVSGELVSVAHALSLPAQSYG
ID172	MADEALFILLHNEMVSG
ID173	MASMQKRLQKELLALQNDPPPGMTLNEKSVQNSITQWIVDMEGAPGTLYEGEKFQLLFKF
m	SSRYPFDSPQVMFTGENIPVHPHVYSNGHICLSILTEDWSPALSVQSVCLSIISMLSSC
ID174	MKXMTGSENWKTKKVLMFCVTPPELET
ID175	MQHIVGVPHVLVRRGLLGRDLFMTRTLCSPGPS
ID176	MYHQSEALALASSQSHLLG
ID177	MSGQGLAGFFASVAMICAIASG

SEQ. ID NO.	SIGNAL PEPTIDE
ID178	MPTGKQLADIGYKTFSTSMMLLTVYGGYLC
ID179	MFPVCLTVTAAVCG
ID180	MSVIFFACVVRVRDG
ID181	MLXGGLKMAPRGKRLSSTPLEILFFLNGWYNATYFLLELFIFLYKGVLLPYPTANLVLDV
	VMLLLYLG
ID182	MIGGGRWDPPGAQAPSSQAFPRRPALTILHLPGTEG
ID183	MVRRVQPDRKQLPLVLLRLLCLLPTGLP
ID184	MPLHYSLVFIIGLVGNLLA
ID185	MARGLGAPHWVAVGLLTWATLGLLVAGLGG

Minimum signal peptide score	false positive rate	false negative rate	proba(0.1)	proba(0.2)
3.5	0.121	0.036	0.467	0.664
4	0.096	0.06	0.519	0.708
4.5	0.078	0.079	0.565	0.745
5	0.062	0.098	0.615	0.782
5.5	0.05	0.127	0.659	0.813
6	0.04	0.163	0.694	0.836
6.5	0.033	0.202	0.725	0.855
7	0.025	0.248	0.763	0.878
7.5	0.021	0.304	0.78	0.889
8	0.015	0.368	0.816	0.909
8.5	0.012	0.418	0.836	0.92
9	0.009	0.512	0.856	0.93
9.5	0.007	0.581	0.863	0.934
10	0.006	0.679	0.835	0.919

**TABLE IV** 

Minimum signal peptide score	All ESTs	New ESTs	ESTs matching public EST closer than 40 bp from beginning	ESTs extending known mRNA more than 40 bp	ESTs extending public EST more than 40 bp
3.5	2674	947	599	23	150
4	2278	784	499	23	126
4.5	1943	647	425	22	112
5	1657	523	353	21	96
5.5	1417	419	307	19	80
6	1190	340	238	18	68
6.5	1035	280	186	18	. 60
7	893		161	15	48
7.5	1	li e	132	12	36
8	1		1 .	11	29
8.5		1	83	1	
9	4		63		
9.5		1	. 48		
10	303	47	35	6	15

TABLE V

•					
Tissue	All ESTs	New ESTs	ESTs matching public EST closer than 40 bp from beginning	ESTs extending known mRNA more than 40 bp	ESTs extending public EST more than 40 bp
Brain	329	131	75	3	24
Cancerous prostate	134	40	37	. 1	6
Cerebellum	17	9	1	0	6
Colon	21	11	4	0	0
Dystrophic muscle	41	18	. 8	0	1
Fetal brain	70	37	16	. 0	1
Fetal kidney	227	116	46	1	19
Fetal liver	13	7	2	- 0	0
Heart	30	15	7	; 0	•
Hypertrophic prostate	86	23	22	<b>'</b> 2	
Kidney	10	7	3	0	0
Large intestine	21	8	4	0	-
Liver	23	9	6	0	
Lung	24	12	4	0	
Lung (cells)	57	38	6	0	-
Lymph ganglia	163	60	23	2	
Lymphocytes	23	6	4	. 0	_
Muscle	33	16	6	0	•
Normal prostate	181	61	45	-	
Ovary	90	57	12	•	
Pancreas	48	11	6	_	
Placenta	24	5	1	0	_
Prostate	. 34	16	4	Q	
Spleen	56	28	10		
Substantia nigra	108	47	27	1	
Surrenals	15	3	_		l (
Testis	131	68	25	1	٤ - ١
Thyroid	17	8		-	-
Umbilical cord	55	17			١ :
Uterus	28				-
Non tissue-specific	568				2 2
Total	2677	947	601	2	3 150

TABLE VI

## Description of Transcription Factor Binding Sites present on promoters isolated from SignalTag sequences

Promoter sequence P13H2 (648 bp):

Matrix	Position	Orientation	Score	Length	Sequence
CMYB_01	-502	•	0.983	ັ 9	TGTCAGTTG
MYOD_Q8	-501	•	0.961	10	CCCAACTGAC
S8_01	-444	• .	0.960	11	AATAGAATTAG
S8_01	-425	+	0.966	11	AACTAAATTAG
DELTAEF1_01	-390	•	0.960	11	GCACACCTCAG
GATA_C	-384	•	0.964	11	AGATAAATCCA
CMYB_01	-349	+	0.958	9	CTTCAGTTG
GATA1_02	-343	<b>◆</b> ;	0.959	14	TTGTAGATAGGACA
GATA_C	-339	•	0.953	11	AGATAGGACAT
TAL1ALPHAE47_01	-235	•	0.973	16	CATAACAGATGGTAAG
TAL1BETAE47_01	-235	•	0.983	16	CATAACAGATGGTAAG
TAL18ETAITF2_01	-235	+	0.978	· 16	CATAACAGATGGTAAG
MYOD_Q6	-232		0.954	10	ACCATCTGTT
· GATA1_04	-217	-	0.953	13	TCAAGATAAAGTA
IK1_01	-126	+	0.963	13	AGTTGGGAATTCC
IK2_01	-126	<b>+</b> .	0.985	12	AGTTGGGAATTC
CREL_01	-123	•	0.962	10	TGGGAATTCC
GATA1_02	-96	•	0.950	14	TCAGTGATATGGCA
SRY_02	-41	-	0.951	12	TAAAACAAAACA
E2F_02	-33	•	0.957	8	TTTAGCGC
MZF1_01	-5	•	<sup>1</sup> 0.975	8	TGAGGGGA

#### Promoter sequence P15B4 (861bp):

Matrix	Position	Orientation	Score	Length	Sequence
NFY_Q6	-748	•	0.956	11	GGACCAATCAT
MZF1_01	-738	+	0.962	8	CCTGGGGA
CMYB_01	-684	•	0.994	9	TGACCGTTG
VMYB_02	-682	•	0.985	. 9	TCCAACGGT
STAT_01	-673	•	0.968	9	TTCCTGGAA
STAT_01	-673	•	0.951	9	TTCCAGGAA
MZF1_01	-556	•	0.956	8	TTGGGGGA
IK2_01	-451	+	0.965	12	GAATGGGATTTC
MZF1_01	-424	•	0.986	. 8	AGAGGGGA
SRY_02	-398	•	0.955	12	GAAAACAAAACA
MZF1_01	-216	+ .	0.960	8	GAAGGGGA
MYOD_Q6	-190	•	0.981	10	AGCATCTGCC
DELTAEF1_01	-176	•	0.958	11	TCCCACCTTCC
S8_01	5	•	0.992	11	GAGGCAATTAT
MZF1_01	16	•	0.986	8	AGAGGGGA

#### Promoter sequence P29B6 (655 bp):

Matrix	Position	Orientation	Score	Length	Sequence
ARNT_01	-311	; <b>+</b>	0.964	16	GGACTCACGTGCTGCT
NMYC_01	-309	• ·	0.965	12	ACTCACGTGCTG
USF_01	-309	•	0.985	- 12	ACTCACGTGCTG
USF_01	-309	•	0.985	12	CAGCACGTGAGT
NMYC_01	-309	•	0.958	12	CAGCACGTGAGT
MYCMAX_02	-309	•	0.972	12	CAGCACGTGAGT
USF_C	-307	•	0.997	8	TCACGTGC
USF_C	-307	•	0.991	8	GCACGTGA
MZF1_01	-292		0.968	8	CATGGGGA
ELK1_02	-105	+	0.963	14	CTCTCCGGAAGCCT
CETS1P54_01	-102	+	0.974	10 -	TCCGGAAGCC
AP1_Q4	-42	•	0.963	11	AGTGACTGAAC
AP1FJ_Q2	-42	•	0.961	11	AGTGACTGAAC
PADS_C	45	+	1.000	9	TGTGGTCTC

15

#### **CLAIMS**

- 1. A purified or isolated nucleic acid comprising the sequence of one of SEQ ID NOs: 38-185 or comprising a sequence complementary thereto.
  - 2. The nucleic acid of Claim 1, wherein said nucleic acid is recombinant.
- 3. A purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 38-185 or one of the sequences complementary thereto.
- 4. A purified or isolated nucleic acid comprising at least 15 consecutive bases of one of the sequences of SEQ ID NOs: 38-185 or one of the sequences complementary thereto.
  - 5. The nucleic acid of Claim 4, wherein said nucleic acid is recombinant.
  - 6. A purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEQ ID NOs: 38-185 or one of the sequences complementary to the sequences of SEQ ID NOs: 38-185.
    - 7. The nucleic acid of Claim 6, wherein said nucleic acid is recombinant.
    - 8. A purified or isolated nucleic acid encoding a human gene product, said human gene product having a sequence partially encoded by one of the sequences of SEQ ID NO: 38-185.
- 9. A purified or isolated nucleic acid having the sequence of one of SEQ ID NOs: 38-185 or having a sequence complementary thereto.
  - 10. A purified or isolated nucleic acid comprising the nucleotides of one of SEQID NOs: 38-185 which encode a signal peptide.
- 11. A purified or isolated polypeptides comprising a signal peptide encoded by one of the sequences of SEQ ID NOs: 38-185.
  - 12. A vector encoding a fusion protein comprising a polypeptide and a signal peptide, said vector comprising a first nucleic acid encoding a signal peptide encoded by one of the sequences of SEQ ID NOs: 38-185 operably linked to a second nucleic acid encoding a polypeptide.
- 30 13. A method of directing the extracellular secretion of a polypeptide or the insertion of a polypetide into the membrane comprising the steps of:

10

20

25

obtaining a vector according to Claim 12; and

introducing said vector into a host cell such that said fusion protein is secreted into the extracellular environment of said host cell or inserted into the membrane of said host cell.

- 14. A method of importing a polypeptide into a cell comprising contacting said cell with a fusion protein comprising a signal peptide encoded by one of the sequences of SEQ ID NOs: 38-185 operably linked to said polypeptide.
- 15. A method of making a cDNA encoding a human secretory protein that is partially encoded by one of SEQ ID NOs 38-185, comprising the steps of:

obtaining a cDNA comprising one of the sequences of SEQ ID NOs: 38-185;

contacting said cDNA with a detectable probe comprising at least 15 consecutive nucleotides of said sequence of SEQ ID NO: 38-185 or a sequence complementary thereto under conditions which permit said probe to hybridize to said cDNA;

identifying a cDNA which hybridizes to said detectable probe; and isolating said cDNA which hybridizes to said probe.

- 15 16. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 15.
  - 17. The cDNA of Claim 16 wherein said cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-185.
    - 18. A method of making a cDNA comprising one of the sequences of SEQ ID NOs: 38-185, comprising the steps of:

contacting a collection of mRNA molecules from human cells with a first primer capable of hybridizing to the polyA tail of said mRNA;

hybridizing said first primer to said polyA tail;

reverse transcribing said mRNA to make a first cDNA strand;

making a second cDNA strand complementary to said first cDNA strand using at least one primer comprising at least 15 nucleotides of one of the sequences of SEQ ID NOs 38-185; and

isolating the resulting cDNA comprising said first cDNA strand and said second cDNA strand.

10

15

20

30

- 19. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 18.
- 20. The cDNA of Claim 19 wherein said cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-185.
  - 21. The method of Claim 18, wherein the second cDNA strand is made by:

contacting said first cDNA strand with a first pair of primers, said first pair of primers comprising a second primer comprising at least 15 consecutive nucleotides of one of the sequences of SEQ ID NOs 38-185 and a third primer having a sequence therein which is included within the sequence of said first primer;

performing a first polymerase chain reaction with said first pair of nested primers to generate a first PCR product;

contacting said first PCR product with a second pair of primers, said second pair of primers comprising a fourth primer, said fourth primer comprising at least 15 consecutive nucleotides of said sequence of one of SEQ ID NO:s 38-185, and a fifth primer, said fourth and fifth primers being capable of hybridizing to sequences within said first PCR product; and

performing a second polymerase chain reaction, thereby generating a second PCR product.

- 22. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185, or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 21.
- 23. The cDNA of Claim 22 wherein said cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-185.
  - 24. The method of Claim 18 wherein the second cDNA strand is made by:
    contacting said first cDNA strand with a second primer comprising at least 15
    consecutive nucleotides of the sequences of SEQ ID NOs: 38-185;

hybridizing said second primer to said first strand cDNA; and extending said hybridized second primer to generate said second cDNA strand.

25

30

- 25. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein partially encoded by one of SEQ ID NOs 38-185 or comprising a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 24.
- 26. The cDNA of Claim 25, wherein said cDNA comprises the full protein coding sequence partially included in of one of the sequences of SEQ ID NOs: 38-185.
- 27. A method of making a protein comprising one of the sequences of SEQ ID NO: 186-333, comprising the steps of:

obtaining a cDNA encoding the full protein sequence partially included in one of the sequences of sequence of SEQ ID NO: 38-185;

inserting said cDNA in an expression vector such that said cDNA is operably linked to a promoter;

introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA; and

isolating said protein.

- 28. An isolated protein obtainable by the method of Claim 27.
- 29. A method of obtaining a promoter DNA comprising the steps of:

obtaining DNAs located upstream of the nucleic acids of SEQ ID NO: 38-185 or the sequences complementary thereto;

screening said upstream DNAs to identify a promoter capable of directing transcription initiation; and

isolating said DNA comprising said identified promoter.

- 30. The method of Claim 29, wherein said obtaining step comprises chromosome walking from said nucleic acids of SEQ ID NO: 38-185 or sequences complementary thereto.
- 31. The method of Claim 30, wherein said screening step comprises inserting said upstream sequences into a promoter reporter vector.
  - 32. The method of Claim 30, wherein said screening step comprises identifying motifs in said upstream DNAs which are transcription factor binding sites or transcription start sites.
    - 33. An isolated promoter obtainable by the method of Claim 32.

- 34. An isolated or purified protein comprising one of the sequences of SEQ ID NO: 186-333.
- 35. In an array of discrete ESTs or fragments thereof of at least 15 nucleotides in length, the improvement comprising inclusion in said array of at least one of the sequences of SEQ ID NOs: 38-185, or one of the sequences complementary to the sequences of SEQ ID NOs: 38-185, or a fragment thereof of at least 15 consecutive nucleotides.
- 36. The array of Claim 35 including therein at least two of the sequences of SEQ ID NOs: 38-185, the sequences complementary to the sequences of SEQ ID NOs: 38-185, or fragments thereof of at least 15 consecutive nucleotides.
- 10 37. The array of Claim 35 including therein at least five of the sequences of SEQ ID NOs: 38-185, the sequences complementary to the sequences of SEQ ID NOs: 38-185, or fragments thereof of at least 15 consecutive nucleotides.

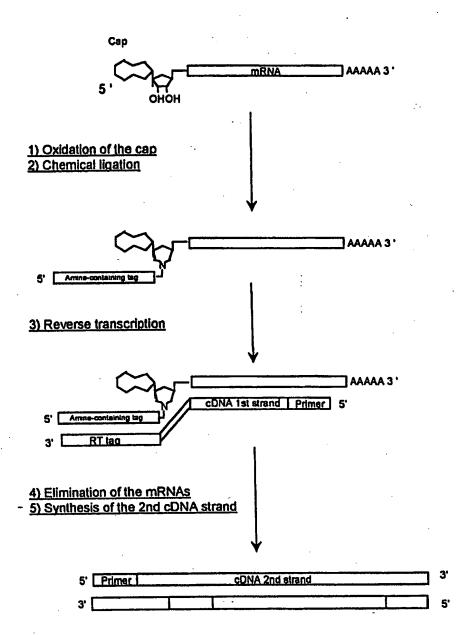


Figure 1

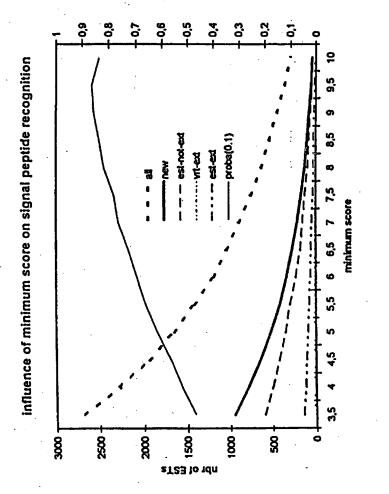


Figure 2

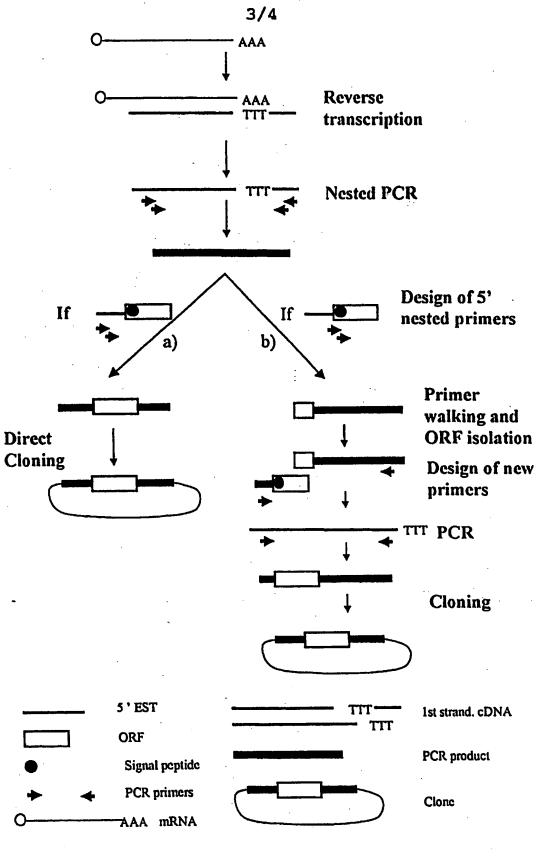
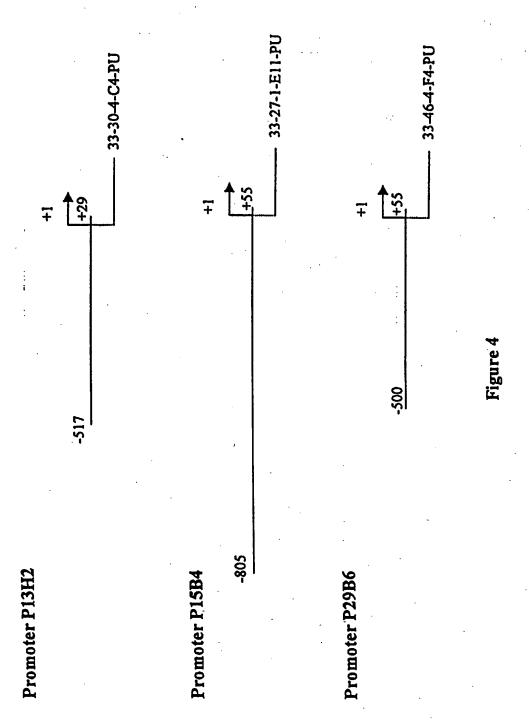


Figure 3



### SEQUENCE LISTING

- (1) GENERAL INFORMATION:
  - (A) NAME: GENSET SA
  - (B) STREET: 24, RUE ROYALE
  - (C) CITY: PARIS
  - (E) COUNTRY: FRANCE
  - (F) POSTAL CODE (ZIP): 75008
  - (ii) TITLE OF INVENTION: 5' ESTS FOR SECRETED PROTEINS EXPRESSED IN VARIOUS TISSUES
  - (iii) NUMBER OF SEQUENCES: 333
  - (v) COMPUTER READABLE FORM:
    - (A) MEDIUM TYPE: Floppy Disk
    - (B) COMPUTER: IBM PC compatible
    - (C) OPERATING SYSTEM: Win95
    - (D) SOFTWARE: Word
- (2) INFORMATION FOR SEQ ID NO: 1:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 47 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: SINGLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Other nucleic acid
  - (ix) FEATURE:
    - (A) NAME/KEY: Cap
    - (B) LOCATION: 1
    - (D) OTHER INFORMATION: m7Gppp added to 1
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

GGCAUCCUAC UCCCAUCCAA UUCCACCCUA ACUCCUCCCA UCUCCAC

- (2) INFORMATION FOR SEQ ID NO: 2:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 46 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: SINGLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Other nucleic acid
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

PCT/IB98/01237

WO	00/0	CEE2
WU	<b>77/</b> ()	10227

(2)	INFORMATION FOR SEQ ID NO: 3:	•
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
	(ii) MOLECULE TYPE: Other nucleic acid	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:	,
ATC	AAGAATT CGCACGAGAC CATTA	25
(2)	INFORMATION FOR SEQ ID NO: 4:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
; i	(ii) MOLECULE TYPE: Other nucleic acid	:
:	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:	:
TAA'	TGGTCTC GTGCGAATTC TTGAT	. 25
(2)	INFORMATION FOR SEQ ID NO: 5:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
	(ii) MOLECULE TYPE: Other nucleic acid	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:	
CCG	ACAAGAC CAACGTCAAG GCCGC	25
(2)	INFORMATION FOR SEQ ID NO: 6:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
	(ii) MOLECULE TYPE: Other nucleic acid	

PCT/IB98/01237

WA	AA.	'n	6553	
wu	44	и.	のつつこ	

3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

TCACCAGCAG GC	AGTGGCTT	AGGAG
---------------	----------	-------

25

- (2) INFORMATION FOR SEQ ID NO: 7:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 25 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: SINGLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Other nucleic acid
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

## AGTGATTCCT GCTACTTTGG ATGGC

25

- (2) INFORMATION FOR SEQ ID NO: 8:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 25 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: SINGLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Other nucleic acid
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

## GCTTGGTCTT GTTCTGGAGT TTAGA

25

- (2) INFORMATION FOR SEQ ID NO: 9:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 25 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: SINGLE
    - (D) TOPOLOGY: LINEAR
    - (ii) MOLECULE TYPE: Other nucleic acid
    - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

## TCCAGAATGG GAGACAAGCC AATTT

- (2) INFORMATION FOR SEQ ID NO: 10:
  - (i) SEQUENCE CHARACTERISTICS:

		-	<del></del> '
WO 99/0655	3	4	PCT/IB98
٠,	(A) LENGTH: 25 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: SINGLE (D) TOPOLOGY: LINEAR		
(ii) M	OLECULE TYPE: Other nucle	ic acid	
(xi) S	EQUENCE DESCRIPTION: SEQ	ID NO: 10:	• ,
agggaggagg a	AACAGCGTG AGTCC		25
(2) INFORMAT	TION FOR SEQ ID NO: 11:		
• •	QUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: SINGLE (D) TOPOLOGY: LINEAR		
(ii) M	OLECULE TYPE: Other nucle	ic acid	
(xi) S	EQUENCE DESCRIPTION: SEQ	ID NO: 11:	
ATGGGAAAGG A	AAAGACTCA TATCA		25
(2) INFORMAT	ION FOR SEQ ID NO: 12:		
	QUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: SINGLE (D) TOPOLOGY: LINEAR		
(ii) M	OLECULE TYPE: Other nucle	ic acid	
(xi) S	EQUENCE DESCRIPTION: SEQ	ID NO: 12:	
AGCAGCAACA A	ATCAGGACAG CACAG		25
•			

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: SINGLE (D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: Other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

25

D	<b>ፈግጥ</b>	AG:	<b>ከጥ</b> ፐ	CGCA	CGAGA	C CATTA

(2) INFORMATION FOR SEQ ID NO: 14:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 67 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: Other nucleic acid	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:	
ATCGTTGAGA CTCGTACCAG CAGAGTCACG AGAGAGACTA CACGGTACTG GTTTTTTTT	60
TTTTVN	67
(2) INFORMATION FOR SEQ ID NO: 15:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 29 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: Other nucleic acid	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:	
CCAGCAGAGT CACGAGAGAG ACTACACGG	29
(2) INFORMATION FOR SEQ ID NO: 16:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: Other nucleic acid	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:	
CACGAGAGAG ACTACACGGT ACTGG	25
(2) INFORMATION FOR SEQ ID NO: 17:	

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 526 base pairs

w ... ...

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (261..376)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 166..281

id N70479

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (380..486)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

region 54..160

id N70479

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(110..145)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 94

region 403..438

id N70479

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (196..229)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 94

region 315..348

id N70479

est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 90..140
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.2

seq LLLITAILAVAVG/FP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

AATATRARAC AGCTACAATA TTCCAGGGCC ARTCACTTGC CATTTCTCAT AACAGCGTCA

60

GAGAGAAAGA ACTGACTGAR ACGTTTGAG ATG AAG AAA GTT CTC CTC CTC ATC Met Lys Lys Val Leu Leu Leu Ile

-15 -

														GAC Asp			161
			-											TCA Ser	GGR Gly	٠	209
											-			CCA Pro	ATT Ile		257
														CCA Pro	ATA Ile 55		305
						ACT Thr							TAA	ACAAI	RAA		354
GGAF	\AAG'	CA C	CRATA	AAACO	CT GO	STCAC	CCTG	AA A	rtga/	TTA	GAGO	CAC	rtc (	CTTG	AARAAT	ì	414
CAA	ATTO	CT (	STTA	LAATA	AA RA	AAAA	ACAA	A TGT	TAAT!	rgaa	ATAC	GCAC	ACA (	GCAT'	CTCTA		474
GTC	AATA	CT 1	[TAG]	rgat(	CT TO	CTTTA	: Aatai	A AC	ATGA	AAGC	AAA	AAAA	AAA 2	AA			526

## (2) INFORMATION FOR SEQ ID NO: 18:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 17 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 1..17
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.2

seq LLLITAILAVAVG/FP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val 1 5 10 15

Gly

- (2) INFORMATION FOR SEQ ID NO: 19:
  - (i) SEQUENCE CHARACTERISTICS:

\*\*\* T

- (A) LENGTH: 822 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

## (ii) MOLECULE TYPE: CDNA

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (D) DEVELOPMENTAL STAGE: Fetal
- (F) TISSUE TYPE: kidney

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 260..464
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96

region 153..357 id H57434

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 118..184
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 98..164

id H57434

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 56..113
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 35..92

id H57434

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 454..485
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 348..379

id H57434

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 118..545
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..428

id N27248

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 65..369
- (C) IDENTIFICATION METHOD: blastn

---

(D) OTHER INFORMATION: identity 98 region 41..345 id H94779 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 61..399 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 6..344 id H09880 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 408..458 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 92 region 355..405 id H09880 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 60..399 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 56..395 id H29351 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 393..432 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 90 region 391..430 id H29351 est (A) NAME/KEY: sig\_peptide (B) LOCATION: 346..408 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 5.5 seq SFLPSALVIWTSA/AF

## (ix) FEATURE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

2	ACTCCTTTTA	GCATAGGGGC	TTCGGCGCCA	GCGGCCAGCG	CTAGTCGGTC	TGGTAAGTGC	60
(	TGATGCCGA	GTTCCGTCTC	TCGCGTCTTT	TCCTGGTCCC	AGGCAAAGCG	GASGNAGATC	120
•	CTCAAACGGC	CTAGTGCTTC	GCGCTTCCGG	AGAAAATCAG	CGGTCTAATT	AATTCCTCTG	180
;	STTTGTTGAA	GCAGTTACCA	AGAATCTTCA	ACCCTTTCCC	ACAAAAGCTA	ATTGAGTACA	240
;	CGTTCCTGTT	GAGTACACGT	TCCTGTTGAT	TTACAAAAGG	TGCAGGTATG	AGCAGGTCTG	300

AAGA	CTA	ACA 1	TTTT	STGA <i>I</i>	AG TI	GTA!	AACA	A GAF	AACO	TGT	TAGA			rp Tr	G TT p Ph	_	357
							CCT Pro -10								TCT Ser	•	405
							ATT Ile										453
							AGT Ser										501
							CTA Leu										549
AAA Lys	TAG	AAAT	CAG (	GAARI	ATAA1	TT C	AACTI	raaac	AA:	(TTC)	ATTT	CATO	GACC?	<b>AAA</b>		٠	602
CTCI	rtcai	RAA I	ACAT	GTCT	T A	CAAGO	CATAT	CTC	CTTG	TTAT	GCT	TCT	ACA (	CTGTT	rgaat	T	662
GTC1	rggci	AAT A	ATTT	CTGC	AG TO	GAA	ATT!	GA:	[ATT]	RMTA	GTT	CTTG!	ACT (	GATA	\ATA1	'G	722
GTA	AGGT	GGG (	CTTT	rccc	CC TO	STGT	AATTO	G GC	CACT	ATGT	CTT	ACTG!	AGC (	CAAG1	TGTA	W	782
TTTC	GAAA'	raa i	aatgi	ATAT(	GA GI	AGTG	ACAC	A AA	\AAA!	AAAA	•			,			822

## (2) INFORMATION FOR SEQ ID NO: 20:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 21 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 1..21
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.5

seq SFLPSALVIWTSA/AF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

Met Trp Trp Phe Gln Gln Gly Leu Ser Phe Leu Pro Ser Ala Leu Val 1 10 15

Ile Trp Thr Ser Ala

(2) INFORMATION FO	R SEQ	ID	NO:	21:
--------------------	-------	----	-----	-----

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 405 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Testis
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(103..398)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 1..296 id AA442893

est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 185..295
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.9

seq LSYASSALSPCLT/AP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

ATCACCTTCT TCTCCATCCT TSTCTGGGCC AGTCCCCARC CCAGTCCCTC TCCTGACCTG	60
CCCAGCCCAA GTCAGCCTTC AGCACGCGCT TTTCTGCACA CAGATATTCC AGGCCTACCT	120
GGCATTCCAG GACCTCCGMA ATGATGCTCC AGTCCCTTAC AAGCGCTTCC TGGATGAGGG	180
TGGC ATG GTG CTG ACC ACC CTC CCC TTG CCC TCT GCC AAC AGC CCT GTG  Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val  -35  -30  -25	229
AAC ATG CCC ACC ACT GGC CCC AAC AGC CTG AGT TAT GCT AGC TCT GCC Asn Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala -20	277
CTG TCC CCC TGT CTG ACC GCT CCA AAK TCC CCC CGG CTT GCT ATG ATG Leu Ser Pro Cys Leu Thr Ala Pro Xaa Ser Pro Arg Leu Ala Met Met -5 10	325
CCT GAC AAC TAAATATCCT TATCCAAATC AATAAARWRA RAATCCTCCC TCCARAAGGG	384

ТТТСТААААА САААААААА А

Pro Asp Asn

#### (2) INFORMATION FOR SEQ ID NO: 22:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 37 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: 1..37
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.9

seq LSYASSALSPCLT/AP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val Asn 1 5 10 15

Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala Leu 20 25 30

Ser Pro Cys Leu Thr 35

- (2) INFORMATION FOR SEQ ID NO: 23:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 496 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Cancerous prostate
    - (ix) FEATURE:
      - (A) NAME/KEY: other
      - (B) LOCATION: 149..331
      - (C) IDENTIFICATION METHOD: blastn
      - (D) OTHER INFORMATION: identity 98 region 1..183 id AA397994

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 328..485
  - (C) IDENTIFICATION METHOD: blastn

(ix)

(ix)

(xi)

			_ =="
53		13	
(0)	OTHER INFORMATION:		36
FEAT	URE:		
(A)	NAME/KEY: other		
(B)	LOCATION: complemen	t(182496)	
(C)	IDENTIFICATION METH	OD: blastn	•
	OTHER INFORMATION:	identity 97 region 14328 id AA399680 est	3
FEAT	URE:		
(A)	NAME/KEY: sig_pepti	de	
	LOCATION: 196240		
	IDENTIFICATION METH		matrix
(D)	OTHER INFORMATION:	score 5.5 seq ILSTVTALTI	FAXA/LD
SEQU	ENCE DESCRIPTION: SE	Q ID NO: 23:	
	•		

AAAAAATTGG TCCCAGTTTT CACCCTGCCG CAGGGCTGGC TGGGGAGGGC AGCGGTTTAG	60
ATTAGCCGTG GCCTAGGCCG TTTAACGGGG TGACACGAGC NTGCAGGGCC GAGTCCAAGG	120
CCCGGAGATA GGACCAACCG TCAGGAATGC GAGGAATGTT TTTCTTCGGA CTCTATCGAG	180
GCACACAGAC AGACC ATG GGG ATT CTG TCT ACA GTG ACA GCC TTA ACA TTT  Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe  -15  -10  -5	231
GCC ARA GCC CTG GAC GGC TGC AGA AAT GGC ATT GCC CAC CCT GCA AGT Ala Xaa Ala Leu Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser 1 5 10	279
GAG AAG CAC AGA CTC GAG AAA TGT AGG GAA CTC GAG ASC ASC CAC TCG Glu Lys His Arg Leu Glu Lys Cys Arg Glu Leu Glu Xaa Xaa His Ser 15 20 25	327
GCC CCA GGA TCA ACC CAS CAC CGA AGA AAA ACA ACC AGA AGA AAT TAT Ala Pro Gly Ser Thr Xaa His Arg Arg Lys Thr Thr Arg Arg Asn Tyr 30 35 40 45	375
TCT TCA GCC TGAAATGAAK CCGGGATCAA ATGGTTGCTG ATCARAGCCC ATATTTAAAT Ser Ser Ala	434
TGGAAAAGTC AAATTGASCA TTATTAAATA AAGCTTGTTT AATATGTCTC AAACAAAAA	494
AA	496

- (2) INFORMATION FOR SEQ ID NO: 24:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 15 amino acids
    - (B) TYPE: AMINO ACID

- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 1..15
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.5.

seq ILSTVTALTFAXA/LD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe Ala Xaa Ala 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 25:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 623 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Testis
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: 49..96
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 10.1

seq LVLTLCTLPLAVA/SA

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:
- AAAGATCCCT GCAGCCCGGC AGGAGAAG GCTGAGCCTT CTGGCGTC ATG GAG AGG 57

  Met Glu Arg
  -15
- CTC GTC CTA ACC CTG TGC ACC CTC CCG CTG GCT GTG GCG TCT GCT GGC

  Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala Ser Ala Gly

  -10

  -5

  105
- TGC GCC ACG ACG CCA GCT CGC AAC CTG AGC TGC TAC CAG TGC TTC AAG

  Cys Ala Thr Tnr Pro Ala Arg Asn Leu Ser Cys Tyr Gln Cys Phe Lys

  5 10 15
- GTC AGC AGC TGG ACG GAG TGC CCG CCC ACC TGG TGC AGC CCG CTG GAC
  Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser Pro Leu Asp
  20 25 30 35

						GAG Glu										249
						CGC Arg										297
						CCG Pro										345
Arg						GCT Ala 90										393
						CRA Xaa										441
			-			GTG Val										489
						CTC Leu										534
TAAG	CACTO	STG (	GTG	ccc	CA CO	CTGT	CAT	r GGG	BACC	ACRA	CTT	CACCO	CTC :	rtgg!	ARACAA	594
TAAI	ACTC	rca :	rgcco	CCA	AA AA	\AAA!	AAAA									623

## (2) INFORMATION FOR SEQ ID NO: 26:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 16 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR.
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 1..16
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 10.1

seq LVLTLCTLPLAVA/SA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

Met Glu Arg Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala 1 5 10 15

(2) INFORMATION FOR	SEO	ID	NO:	27:
---------------------	-----	----	-----	-----

(1)	SEOUENCE	CHARA	CTERI	STICS:

- (A) LENGTH: 848 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

# (ii) MOLECULE TYPE: CDNA

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (D) DEVELOPMENTAL STAGE: Fetal
- (F) TISSUE TYPE: kidney

# (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 32..73
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 10.7

seq LWLLFFLVTAIHA/EL

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

AACTTTGCCT TGTGTTTTCC ACCCTGAAAG A ATG TTG TGG CTG CTC TTT TTT CTG  Met Leu Trp Leu Leu Phe Phe Leu  -10	55
GTG ACT GCC ATT CAT GCT GAA CTC TGT CAA CCA GGT GCA GAA AAT GCT Val Thr Ala Ile His Ala Glu Leu Cys Gln Pro Gly Ala Glu Asn Ala -5 10	103
TTT AAA GTG AGA CTT AGT ATC AGA ACA GCT CTG GGA GAT AAA GCA TAT Phe Lys Val Arg Leu Ser Ile Arg Thr Ala Leu Gly Asp Lys Ala Tyr 15 20 25	151
GCC TGG GAT ACC AAT GAA GAA TAC CTC TTC AAA GCG ATG GTA GCT TTC Ala Trp Asp Thr Asn Glu Glu Tyr Leu Phe Lys Ala Met Val Ala Phe 30 35 40	199
TCC ATG AGA AAA GTT CCC AAC AGA GAA GCA ACA GAA ATT TCC CAT GTC Ser Met Arg Lys Val Pro Asn Arg Glu Ala Thr Glu Ile Ser His Val 45 50 55	247
CTA CTT TGC AAT GTA ACC CAG AGG GTA TCA TTC TGG TTT GTG GTT ACA Leu Leu Cys Asn Val Thr Gln Arg Val Ser Phe Trp Phe Val Val Thr 60 65 70	295
GAC CCT TCA AAA AAT CAC ACC CTT CCT GCT GTT GAG GTG CAA TCA GCC Asp Pro Ser Lys Asn His Thr Leu Pro Ala Val Glu Val Gln Ser Ala 75 80 85 90	343
ATA AGA ATG AAC AAG AAC CGG ATC AAC AAT GCC TTC TTT CTA AAT GAC Ile Arg Met Asn Lys Asn Arg Ile Asn Asn Ala Phe Phe Leu Asn Asp 95 100 105	391
CAA ACT CTG GAA TTT TTA AAA ATC CCT TCC ACA CTT GCA CCA CCC ATG Gln Thr Leu Glu Phe Leu Lys Ile Pro Ser Thr Leu Ala Pro Pro Met 110 115 120	439

GAC CCA TCT GTG CCC ATC TGG ATT ATT ATA TTT GGT GTG ATA TTT TGC Asp Pro Ser Val Pro Ile Trp Ile Ile Ile Phe Gly Val Ile Phe Cys 125 130 135	487
ATC ATC ATA GTT GCA ATT GCA CTA CTG ATT TTA TCA GGG ATC TGG CAA  Ile Ile Ile Val Ala Ile Ala Leu Leu Ile Leu Ser Gly Ile Trp Gln  140 145 150	535
CGT ADA ARA AAG AAC AAA GAA CCA TCT GAA GTG GAT GAC GCT GAA RAT Arg Xaa Xaa Lys Asn Lys Glu Pro Ser Glu Val Asp Asp Ala Glu Xaa 155 160 165 170	583
AAK TGT GAA AAC ATG ATC ACA ATT GAA AAT GGC ATC CCC TCT GAT CCC Xaa Cys Glu Asn Met Ile Thr Ile Glu Asn Gly Ile Pro Ser Asp Pro 175 180 185	631
CTG GAC ATG AAG GGA GGG CAT ATT AAT GAT GCC TTC ATG ACA GAG GAT Leu Asp Met Lys Gly Gly His Ile Asn Asp Ala Phe Met Thr Glu Asp 190 195 200	679
GAG AGG CTC ACC CCT CTC TGAAGGGCTG TTGTTCTGCT TCCTCAARAA Glu Arg Leu Thr Pro Leu 205	727
ATTAAACATT TGTTTCTGTG TGACTGCTGA GCATCCTGAA ATACCAAGAG CAGATCATAT	787
WTTTTGTTTC ACCATTCTTC TTTTGTAATA AATTTTGAAT GTGCTTGAAA AAAAAAAAAA	847
С	848

## (2) INFORMATION FOR SEQ ID NO: 28:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 14 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 1..14
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 10.7

seq LWLLFFLVTAIHA/EL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

Met Leu Trp Leu Leu Phe Phe Leu Val Thr Ala Ile His Ala 1 5 10

- (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: SINGLE (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: Other nucleic acid
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

#### GGGAAGATGG AGATAGTATT GCCTG

25

- (2) INFORMATION FOR SEQ ID NO: 30:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 26 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: SINGLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Other nucleic acid
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

#### CTGCCATGTA CATGATAGAG AGATTC

- (2) INFORMATION FOR SEQ ID NO: 31:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 546 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (11) MOLECULE TYPE: Genomic DNA
  - (ix) FEATURE:
    - (A) NAME/KEY: promoter (B) LOCATION: 1..517
  - (ix) FEATURE:
    - (A) NAME/KEY: transcription start site
    - (B) LOCATION: 518
  - (ix) FEATURE:
    - (A) NAME/KEY: TF binding-site
    - (B) LOCATION: 17..25
    - (C) IDENTIFICATION METHOD: matinspector prediction
    - (D) OTHER INFORMATION: name CMYB\_01 score 0.983 sequence TGTCAGTTG
  - (ix) FEATURE:
    - (A) NAME/KEY: TF binding-site

. (B) LOCATION: complement(18..27)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name MYOD\_Q6
score 0.961
sequence CCCAACTGAC

## (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement (75..85)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name S8\_01
score 0.960
sequence AATAGAATTAG

#### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 94..104

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name S8\_01
score 0.966
sequence AACTAAATTAG

#### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement (129..139)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name DELTAEF1\_01
score 0.960
sequence GCACACCTCAG

#### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement(155..165)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name GATA\_C score 0.964 sequence AGATAAATCCA

### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 170..178

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name CMYB\_01
score 0.958
sequence CTTCAGTTG

## (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 176..189

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name GATA1\_02
score 0.959
sequence TTGTAGATAGGACA

#### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 180..190

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name GATA\_C score 0.953 sequence AGATAGGACAT

\*\*\* \*\*\*

## (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 284..299

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name TAL1ALPHAE47 01

score 0.973

sequence CATAACAGATGGTAAG

# (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 284..299

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name TAL1BETAE47\_01

score 0.983
sequence CATAACAGATGGTAAG

## (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 284..299

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name TAL1BETAITF2\_01 score 0.978

sequence CATAACAGATGGTAAG

## (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement (287..296)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name MYOD Q6 score 0.954

sequence ACCATCTGTT

### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement (302..314)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name GATA1\_04
score 0.953
sequence TCAAGATAAAGTA

## (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 393..405

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name IK1\_01 score 0.963

sequence AGTTGGGAATTCC

### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 393..404

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name IK2\_01 score 0.985

sequence AGTTGGGAATTC

## (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 396..405

(C) IDENTIFICATION METHOD: matinspector prediction

· water

(D) OTHER INFORMATION: name CREL\_01
score 0.962
sequence TGGGAATTCC

#### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 423..436

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name GATA1\_02 score 0.950

sequence TCAGTGATATGGCA

#### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement (478..489)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name SRY\_02 score 0.951

sequence TAAAACAAAACA

#### (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 486..493

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name E2F\_02
score 0.957
sequence TTTAGCGC

## (ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement (514..521)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name MZF1\_01 score 0.975 sequence TGAGGGGA

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

TGAGTGCAGT GTTACATGTC AGTTGGGTTA AGTTTGTTAA TGTCATTCAA ATCTTCTATG 60

TCTTGATTTG CCTGCTAATT CTATTATTC TGGAACTAAA TTAGTTTGAT GGTTCTATTA 120

GTTATTGACT GAGGTGTGCT AATCTCCCAT TATGTGGATT TATCTATTC TTCAGTTGTA 180

GATAGGACAT TGATAGATAC ATAAGTACCA GGACAAAAGC AGGGAGATCT TTTTTCCAAA 240

ATCAGGAGAA AAAAATGACA TCTGGAAAAC CTATAGGGAA AGGCATAACA GATGGTAAGG 300

ATACTTTATC TTGAGTAGGA GAGCCTTCCT GTGGCAACGT GGAGAAGGGA AGAGGTCGTA 360

GAATTGAGGA GTCAGCTCAG TTAGAAGCAG GGAGTTGGGA ATTCCGTTCA TGTGATTTAG 420

CATCAGTGAT ATGGCAAATG TGGGACTAAG GGTAGTGATC AGAGGGTTAA AATTGTGTGT 480

TTTGTTTTAG CGCTGCTGGG GCATCGCCTT GGGTCCCCTC AAACAGATTC CCATGAATCT 540

CTTCAT

PCT/IB98/01237

· ...

## (2) INFORMATION FOR SEQ ID NO: 32:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 23 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: SINGLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: Other nucleic acid
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

## GTACCAGGGA CTGTGACCAT TGC

23

- (2) INFORMATION FOR SEQ ID NO: 33:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 24 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: SINGLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Other nucleic acid
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

## CTGTGACCAT TGCTCCCAAG AGAG

24

- (2) INFORMATION FOR SEQ ID NO: 34:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 861 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Genomic DNA
  - (ix) FEATURE:
    - (A) NAME/KEY: promoter
    - (B) LOCATION: 1..806
  - (ix) FEATURE:
    - (A) NAME/KEY: transcription start site
    - (B) LOCATION: 807
  - (ix) FEATURE:
    - (A) NAME/KEY: TF binding-site
    - (B) LOCATION: complement (60..70)
    - (C) IDENTIFICATION METHOD: matinspector prediction
    - (D) OTHER INFORMATION: name NFY Q6 score 0.956

sequence GGACCAATCAT

(ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 70..77
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name MZF1\_01 score 0.962 sequence CCTGGGGA

# (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 124..132
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name CMYB\_01
  score 0.994
  sequence TGACCGTTG

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement(126..134)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name VMYB\_02
  score 0.985
  sequence TCCAACGGT

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 135..143
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name STAT\_01 score 0.968 sequence TTCCTGGAA

### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement (135..143)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name STAT\_01 score 0.951 sequence TTCCAGGAA

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement (252..259)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name MZF1\_01 score 0.956 sequence TTGGGGGA

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 357..368
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name IK2\_01
  score 0.965
  sequence GAATGGGATTTC

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 384..391
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name MZF1\_01 score 0.986

-E 3- W

## sequence AGAGGGGA

(ix)	FEATURE:
------	----------

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement (410..421)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name SRY 02 score 0.955

sequence GAAAACAAAACA

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 592..599
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name MZF1 01 score 0.960 sequence GAAGGGGA

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 618..627
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name MYOD Q6 score 0.981

sequence AGCATCTGCC

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 632..642
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name DELTAEF1 01 score 0.958 sequence TCCCACCTTCC

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement(813..823)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name S8\_01 score 0.992 sequence GAGGCAATTAT

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement (824..831)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name MZF1 01 score 0.986 sequence AGAGGGGA

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

TACTATAGGG CACGCGTGGT CGACGGCCGG GCTGTTCTGG AGCAGAGGGC ATGTCAGTAA TGATTGGTCC CTGGGGAAGG TCTGGCTGGC TCCAGCACAG TGAGGCATTT AGGTATCTCT 120 180 CTCAGAGGGC TAGGCACGAG GGAAGGTCAG AGGAGAAGGS AGGSARGGCC CAGTGAGARG

GG	AGCATGCC.	TTCCCCCAAC	CCTGGCTTSC	YCTTGGYMAM	AGGGCGKTTY	TGGGMACTTR	300
AA'	YTCAGGGC	CCAASCAGAA	SCACAGGCCC	AKTCNTGGCT	SMAAGCACAA	TAGCCTGAAT	360
GG	GATTTCAG	GTTAGNCAGG	GTGAGAGGGG	AGGCTCTCTG	GCTTAGTTTT	GTTTTGTTTT	420
CC	AAATCAAG	GTAACTTGCT	CCCTTCTGCT	ACGGGCCTTG	GTCTTGGCTT	GTCCTCACCC	480
AGʻ	ICGGAACT	CCCTACCACT	TTCAGGAGAG	TGGTTTTAGG	CCCGTGGGGC	TGTTCTGTTC	540
CA	AGCAGTGT	GAGAACATGĞ	CTGGTAGAGG	CTCTAGCTGT	GTGCGGGGCC	TGAAGGGGAG	600
TG	GGTTCTCG	CCCAAAGAGC	ATCTGCCCAT	TTCCCACCTT	CCCTTCTCCC	ACCAGAAGCT	660
TG	CCTGAGCT	GTTTGGACAA	AAATCCAAAC	CCCACTTGGC	TACTCTGGCC	TGGCTTCAGC	720
TT(	GGAACCCA	ATACCTAGGC	TTACAGGCCA	TCCTGAGCCA	GGGGCCTCTG	GAAATTCTCT	780
TC	CTGATGGT	CCTTTAGGTT	TGGGCACAAA	ATATAATTGC	СТСТССССТС	TCCCATTTTC	840
TC'	ICTTGGGA	GCAATGGTCA	С		•		861

## (2) INFORMATION FOR SEQ ID NO: 35:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 20 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: SINGLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: Other nucleic acid
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

CTGGGATGGA AGGCACGGTA

20

## (2) INFORMATION FOR SEQ ID NO: 36:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 20 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: SINGLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: Other nucleic acid
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

GAGACCACAC AGCTAGACAA

- (2) INFORMATION FOR SEQ ID NO: 37:
  - (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 555 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: Genomic DNA
- (ix) FEATURE:
  - (A) NAME/KEY: promoter
  - (B) LOCATION: 1..500
- (ix) FEATURE:
  - (A) NAME/KEY: transcription start site
  - (B) LOCATION: 501
- (ix) FEATURE:
  - (A) NAME/KEY: TF binding-site
  - (B) LOCATION: 191..206
  - (C) IDENTIFICATION METHOD: matinspector prediction
  - (D) OTHER INFORMATION: name ARNT\_01
    score 0.964
    sequence GGACTCACGTGCTGCT
- (ix) FEATURE:
  - (A) NAME/KEY: TF binding-site
  - (B) LOCATION: 193..204
  - (C) IDENTIFICATION METHOD: matinspector prediction
  - (D) OTHER INFORMATION: name NMYC\_01
    score 0.965
    sequence ACTCACGTGCTG
- (ix) FEATURE:
  - (A) NAME/KEY: TF binding-site
  - (B) LOCATION: 193..204
  - (C) IDENTIFICATION METHOD: matinspector prediction
  - (D) OTHER INFORMATION: name USF\_01
    score 0.985
    sequence ACTCACGTGCTG
- (ix) FEATURE:
  - (A) NAME/KEY: TF binding-site
  - (B) LOCATION: complement(193..204)
  - (C) IDENTIFICATION METHOD: matinspector prediction
  - (D) OTHER INFORMATION: name USF\_01
    score 0.985
    sequence CAGCACGTGAGT
- (ix) FEATURE:
  - (A) NAME/KEY: TF binding-site
  - (B) LOCATION: complement (193..204)
  - (C) IDENTIFICATION METHOD: matinspector prediction
  - (D) OTHER INFORMATION: name NMYC\_01
    score 0.956
    sequence CAGCACGTGAGT
- (ix) FEATURE:
  - (A) NAME/KEY: TF binding-site
  - (B) LOCATION: complement(193..204)
  - (C) IDENTIFICATION METHOD: matinspector prediction
  - (D) OTHER INFORMATION: name MYCMAX\_02 score 0.972

## sequence CAGCACGTGAGT

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 195..202
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name USF\_C score 0.997 sequence TCACGTGC

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement (195..202)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name USF\_C score 0.991 sequence GCACGTGA

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement (210..217)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name MZF1\_01
  score 0.968
  sequence CATGGGGA

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 397..410
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name ELK1\_02
  score 0.963
  sequence CTCTCCGGAAGCCT

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 400..409
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name CETS1P54\_01 score 0.974 sequence TCCGGAAGCC

### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement (460..470)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name AP1\_Q4 score 0.963 sequence AGTGACTGAAC

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement (460..470)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name AP1FJ\_Q2
  score 0.961
  sequence AGTGACTGAAC

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (3) LOCATION: 547..555

,	(C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name PADS_C score 1.000 sequence TGTGGTCTC	
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 37:	
CTATAGGGCA	CGCKTGGTCG ACGGCCCGGG CTGGTCTGGT CTGTKGTGGA GTCGGGTTGA	60
AGGACAGCAT	TTGTKACATC TGGTCTACTG CACCTTCCCT CTGCCGTGCA CTTGGCCTTT	120
KAWAAGCTCA	GCACCGGTGC CCATCACAGG GCCGGCAGCA CACACATCCC ATTACTCAGA	180
AGGAACTGAC	GGACTCACGT GCTGCTCCGT CCCCATGAGC TCAGTGGACC TGTCTATGTA	240
GAGCAGTCAG	ACAGTGCCTG GGATAGAGTG AGAGTTCAGC CAGTAAATCC AAGTGATTGT	300
CATTCCTGTC	TGCATTAGTA ACTCCCAACC TAGATGTGAA AACTTAGTTC TTTCTCATAG	360
GTTGCTCTGC	CCATGGTCCC ACTGCAGACC CAGGCACTCT CCGGAAGCCT GGAAATCACC	420
CGTGTCTTCT	GCCTGCTCCC GCTCACATCC CACACTTGTG TTCAGTCACT GAGTTACAGA	480
TTTTGCCTCC	TCAATTTCTC TTGTCTTAGT CCCATCCTCT GTTCCCCTGG CCAGTTTGTC	540
TAGCTGTGTG	GTCTC	555
(ii) (ii) (vi)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 247 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  MOLECULE TYPE: CDNA  ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Umbilical cord  FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 152193 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 11.8  seq VLVALILLHSALA/QS  SEQUENCE DESCRIPTION: SEQ ID NO: 38:	
AAAACCAGCG	CCCCGAGTTG AGGCGCGGGT TTGGTGGCGC GTTTCAGCGA AGTCGCACGT	60
GAAGGATAGC	AGTGGCCTGA GAAAGACCCA GTCATGGCAG CCTCCAGCAT CAGTTCACCA	120

TGGRGGAAAG CATGTGTTCA AAGCCATTCT G ATG GTC CTA GTG GCC CTT ATC

Met Val Leu Val Ala Leu Ile

Leu Leu His Ser Ala Leu Ala Gln Ser Arg Arg Asp Phe Ala Pro Pro -5 1 5	220
GGC CAA CAG AAG AGA GAA GCC CCG GGG Gly Gln Gln Lys Arg Glu Ala Pro Gly 10 15	247
(2) INFORMATION FOR SEQ ID NO: 39:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 301 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Lymph ganglia</li></ul>	
(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 98160  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 10  seq LLLCLQTWPEAAG/KD	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:	
AAAATGTCGT TATAAAAAGG AGGAAGAAAA CTCAAGTGAA ACTGACTCTG CTAGAACAGT	60
GCCGTGCTTT TCCACAGAAG GTTAGACCCT GAAAGAG ATG GCT CAG CAC CTA Met Ala Gln His His Leu -20	115
TGG ATC TTG CTC CTT TGC CTG CAA ACC TGG CCG GAA GCA GCT GGA AAA  Trp Ile Leu Leu Cys Leu Gln Thr Trp Pro Glu Ala Ala Gly Lys -15 -5 1	163
GAC TCA GAA ATC TTC ACA GTG AAT GGG ATT CTG GGA GAG TCA GTC ACT Asp Ser Glu Ile Phe Thr Val Asn Gly Ile Leu Gly Glu Ser Val Thr 5 10 15	211
TTC CCT GTA AAT ATC CAA GAA CCA CGG CAA GTT AAA ATC ATT GCT TGG Pne Pro Val Asn Ile Gln Glu Pro Arg Gln Val Lys Ile Ile Ala Trp 20 25 30	259
ACT TCT AAA ACA TCT GTT GCT TAT GTA ACA CCA GGA GAA CGG Thr Ser Lys Thr Ser Val Ala Tyr Val Thr Pro Gly Glu Arg 35 40 45	301

.m. –E.	<b>&gt;-</b> _											-	-			
W	O 99/	06553	3					·	30			•		•	PCT	/IB98/0
	<b>i</b> )	.) SE	EQUE	ICE (	CHARA	ACTE	RIST	cs:						÷		
					TH:				irs							
			(B)	TYPE	E: NC	CLE	CAC	CID								
					NDEL				E							
			(D)	TOPO	DLOGY	: Ll	NEAF	₹							٠	
	i)	.i) N	10LEC	CULE	TYPE	E: CI	ANC									
	(7	ri) (	ORIG	NAL	SOUF	RCE:										
			(A)	ORGA	NISM	1: Hc	omo S	Sapie	ens	•		•				
			(F)	TISS	OE I	YPE:	Lyn	iph c	gangl	ia						
	(i	.x) E	EATU	JRE:												
					:/KEY				ie							
					TION											
					TIFI						_	ie ma	tri	•		
			(U)	OTHE	R IN	IFORM	IATIC	IN:	scor					_		
									seq	FILL	VTAL	RCII	.s/Q/	7		
	ίx	i) S	SEOUE	INCE	DESC	RIPI	ION:	SEC	O I O	NO:	40:					
	, -	, -														
AATI	TTTT	CT 1	CAAA1	TCAC	GG G1	rccc	SCTC	A CA	rgggi	TAAF	ACT:	TTCT	GAG 1	AGTC	CTCGAC	60
CTCC	GGCG	TA A	AGAAC												G ACA	111
				мет	: rA	s As	i re			e Phe	e Le	ı Leı			l Thr	
								-15	•				-10	,		
GCT	CCC	AGA	TGC	ATC	CTG	TCC	CAG	GTG	CAG	CTG	CAG	GAG	TCG	GGC	CCG	159
					Leu											133
		-5	-1-				1				5			1		
											_					
CGT	CTA	GTT	AGG	CCC	TCG	GAG	ACC	GTG	TCC	CTC	AGC	TGC	ACC	GTC	TCC	207
Arg	Leu	Val	Arg	Pro	Ser	Glu	Thr	Val	Ser	Leu	Ser	Cys	Thr	Val	Ser	
10					15					20					25	
					AGT											255
Gly	Asp	Ser	Val		Ser	Gly	Asp	His	_	Trp	Thr	Trp	Leu		Gln	
				30					35					40		
CCC	CCC	ccc	ccc	CCA	CTG	CAC	TCC	ልጥጥ	ccc	<b>יי</b> מיד	እጥ <b>ር</b>	TAC	»cc	аст	ccc	303
					Leu											303
		<b>4-</b> 3	45	<b>U</b> _J				50	4-1	- ] -		-1-	55		CLY	
AAA	ATC	GAC	TAC	AAC	CCC	TCS	MTC	AGG	CGT	CGA	GTC	ACC	ATC	TCC	GTG	351
					Pro											
-		60	-				65	•		•		70	•			
									•							
					CTT								- '			384
Asp	Thr	Ser	Lys	Asn	Leu	Phe	Ser	Leu	Thr	Arg						
	75					80										
																_
																•

- (2) INFORMATION FOR SEQ ID NO: 41:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 296 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR

99/06553	31		PCT/IB98/01237
(ii) MOLECULE TYPE: CDNA			
(vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sap (F) TISSUE TYPE: Place		·	

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 60..122
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 10

seq LLLCLQTWPEAAG/KD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

AAACTGACTC TG	CTAGAACA GTGCC	GTGCT TTTCCACAGA	AGGTTAGACC CTGAAAGAG	59
ATG GCT CAG CAMET Ala Gln H: -20	AC CAC CTA TGG is His Leu Trp -15	Ile Leu Leu Leu	TGC CTG CAA ACC TGG Cys Leu Gln Thr Trp -10	107
			ACA GTG AAT GGG ATT Thr Val Asn Gly Ile 10	155
Leu Gly Glu Se	CA GTC ACT TTC er Val Thr Phe 15	CCT GTA AAT ATC Pro Val Asn Ile 20	CAA GAA CCA CGG CAA Gln Glu Pro Arg Gln 25	203
			GTT GCT TAT GTA ACA Val Ala Tyr Val Thr 40	251
		CCC GTA GTT ACT Pro Val Val Thr		296

## (2) INFORMATION FOR SEQ ID NO: 42:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 232 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens.
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 59..115
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9.9

seq FLFVVAAATGVQS/QV

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

ATC	ACAT	AAC A	ATCC!	ACAT	CT CT	CCT	CTGA	A GA	AGGC	CCTG	GGA	GCGC	AST (	CANTO	CACC	. 58
ATG Met	GAC Asp	TGG Trp	ACC Thr	TGG Trp -15	AGG Arg	TTC Phe	CTC Leu	TTT Phe	GTG Val -10	GTG Val	GCA Ala	GCA Ala	GCT Ala	ACA Thr -5	GGT Gly	106
GTC Val	CAG Gln	TCT Ser	CAG Gln 1	GTT Val	CAA Gln	CTG Leu	GTG Val 5	CAA Gln	TCT Ser	GGG Gly	GCT Ala	GĀG Glu 10	GTG Val	GTG Val	AAG Lys	154
CCT Pro	GGG Gly 15	TCC Ser	TCG Ser	GTA Val	AAG Lys	GTC Val 20	TCC Ser	TGT Cys	AAG Lys	ACT Thr	TCT Ser 25	GGA Gly	GAC Asp	GGT Gly	TTC Phe	202
					AAC Asn 35						·					232

## (2) INFORMATION FOR SEQ ID NO: 43:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 290 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 105..161
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9.6

seq GLLLLCLLPHRLA/LV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

ACACCATDTG CTTTAGTTTC AGTCCTCGTA TCATAGAAAA GTTCATGTCA TAAAAGAAGT	60
TAAAACCACT CTTGAATAAT TGGAACCCTT ATGCCAATTG TCTA ATG TCA ATT TGT Met Ser Ile Cys	116
TTT CTG GGA TTG CTT CTT CTA TGT CTT CCT CAT CGT CTG GCA CTG Phe Leu Gly Leu Leu Leu Cys Leu Leu Pro His Arg Leu Ala Leu -15 -5 1	164
GTT CAG AAA CAC TCA TCT CCA TCA AGT CGT CTT CTG CTA ATT CCT GTG Val Gln Lys His Ser Ser Pro Ser Ser Arg Leu Leu Ile Pro Val 5 10 15	212

WO 99/06553	33 PCT/I	B98/0
	CTA GCT CTT GAA TTT CTC CAA GAT CCA TAT CTT GAT Leu Ala Leu Glu Phe Leu Gln Asp Pro Tyr Leu Asp 25 30	260
	CCC CTG CCC CCA CCT TGG Pro Leu Pro Pro Pro Trp 40	290
(2) INFORMATION	FOR SEQ ID NO: 44:	
(A) (B) (C)	NCE CHARACTERISTICS: LENGTH: 213 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLEC	CULE TYPE: CDNA	
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Lymph ganglia	
(B) (C)	NAME/KEY: sig_peptide LOCATION: 148198 IDENTIFICATION METHOD: Von Heijne matrix OTHER INFORMATION: score 9.2 seq LVLLILPLLSSLS/KV	: :
(xi) SEQUI	ENCE DESCRIPTION: SEQ ID NO: 44:	
ATTTCTCTAA ACAG	CTTGTT ACATGTTCCT TTTAAGTTCA GTCAAATTGC ATAGGAACTT	60
ATTTTTAAGT AGAA	GATAGA TTCTGAAGCT TTATGTATAC GGATTAAAAA TTGAGGCTAA	120
AATTTGATCT TATT	TTAACT TTATAAT ATG ATA GGA TTT CTA GTG CTT TTA ATA  Met Ile Gly Phe Leu Val Leu Leu Ile  -15 -10	174
	TCT TCC TTA TCC AAA GTC AGC TCC AAG Ser Ser Leu Ser Lys Val Ser Ser Lys 1 5	213
(2) INFORMATION	FOR SEQ ID NO: 45:	
(A) (B)	NCE CHARACTERISTICS: LENGTH: 175 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE	

(D) TOPOLOGY: LINEAR

(A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Lymph ganglia

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(ix) FEATURE:

<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide</pre>	
(B) LOCATION: 59151	
(C) IDENTIFICATION METHOD: Von Heijne matrix	
(D) OTHER INFORMATION: score 8.9 seq LLMSLLVSTVTWQ/IS	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:	
(XI) SEQUENCE DESCRIPTION. SEQ ID NO. 45.	
ATTTTTTAA CATTGTCAAG CTTTATATCA TGTTATTTCC CAAGTATAAT TCACATGG	58
The state of the s	106
Met Gln Cys Leu Leu Ser Val Leu Met Ala Gln Phe Ile Xaa His Phe -30 -25 -20	
	154
Leu Ser Leu Leu Met Ser Leu Leu Val Ser Thr Val Thr Trp Gln Ile -15 -5 1	•
	175
Ser Arg Thr Pro Trp His Gly 5	
(2) INFORMATION FOR SEQ ID NO: 46:	
(i) SEQUENCE CHARACTERISTICS:	
(A) LENGTH: 341 base pairs (B) TYPE: NUCLEIC ACID	
(C) STRANDEDNESS: DOUBLE	
(D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
(vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens	
(F) TISSUE TYPE: Lymph ganglia	
(ix) FEATURE:	
(A) NAME/KEY: sig_peptide (B) LOCATION: 81137	
(C) IDENTIFICATION METHOD: Von Heijne matrix	
(D) OTHER INFORMATION: score 8.9 seq WIFFLATLKGVQC/QV	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:	
ACCTCTGGGA GAGGAGCCCC AGCCCTGAGA TCCCCGGGTG TTTCCATTCA GCGACCAGCA	60
	113
Met Glu Leu Gly Leu Ser Trp Ile Phe Phe Leu -15 -10	
GCT ACT TTA AAA GGT GTC CAA TGT CAG GTG AGG CTG CTG GAG TCT GCG	161
Ala Thr Leu Lys Gly Val Gln Cys Gln Val Arg Leu Leu Glu Ser Ala	

			GGC Gly 15					209
			GAC Asp					257
			TGG Trp					305
			TCT Ser				, 2	341

#### (2) INFORMATION FOR SEQ ID NO: 47:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 195 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 19..63
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.6

seq SVSLALLSGWVGS/RQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

ACCO	TTTC	CC 1	GTT	AGAC		GTA Val										51
						GGT Gly										99
•		2		í		,4		5	1				.10			
						TGC Cys										147
200	<b>41</b>	15	,,,,	-		0,0	20	•••		Val	nry	25	O.I.I	AIG	рец	
						AAA										195
GLÜ	30	rne	neu	ser	val	Lys 35		ıyı	ser	ATG	Pne 40	ser	ATA	Asp	GIU	

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 342 base pairs(B) TYPE: NUCLEIC ACID

				STRA TOPO												
	(i	i) M	OLEC	ULE	TYPE	: CI	ANC									
	- ( <u>v</u>	i) C	(A)	NAL ORGA TISS	NISM	I: Ho										
	(i	x) F	(B) (C)	IRE: NAME LOCA IDEN OTHE	TION TIFI	: 17 CATI	22 ON M	34 IETHO	D: V	е 8.						
	(x	i) S	EQUE	NCE	DESC	RIPT	:NOI	SEC	) ID	NO:	48:					
AGC	GTGC	CT G	GCC1	rccc	CT CC	CAG	ACTGO	C AGO	GACA	AGCA	ccc	GTA	ACT (	CGA	STGGAG	60
CGGA	GGAC	cc e	AGC	GCT	A GO	SAGA	SAGGA	A GGC	CGGCC	GCT	TAGO	TGC	PAC C	GGG1	CCGGC	120
CGGC	GCCC	TC C	CCGAC	GGGG	G CI	CAG	GAGG <i>I</i>	A GG!	AAGGA	AGGA	ccc	TGC	GAG A		CCT Pro -20	177
				CTT Leu -15												225
				GCG Ala												273
				GGG Gly												321
				AGA Arg												342
													_			-
(2)	INFO	ORMA!	rion	FOR	SEQ	ID	NO:	49:								

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 377 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens

- -

(F) TISSUE TYPE: Lymph ganglia

•	i.x	١	FΕ	ď	וזיז	RE	

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 36..275
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 8.4

seq FVVFSLFLICAMA/GD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

AGCA	\GAA#	AC 1	CAACT	GAA	A AC	GAGA	ACCT	C ACT	GT F	NTG G	STT F	AGT F	L TAL	TC I	TC	53
										et V -80	/al S	Ser F	lsn E	Phe E	he 75	
					TTC Phe											101
					GTC Val											149
					AAA Lys											197
					GAT Asp											245
					ATC Ile -5											293
					CGG Arg											341
					TTC Phe											377

# (2) INFORMATION FOR SEQ ID NO: 50:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 240 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE: .
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:

144

192

240

V	VO 99	/0655	3		•				38	3					P
				NAME					le						
			. – ,	LOCA											
			(C)	IDEN	TIFI	CATI	ON M	ETHO	D: V	on b	leijr	ne ma	trix	•	
			(D)	OTHE	RIN	FORM	IATIC	N:	SCOI	ce 8.	2				
			• • •	•					seq	ICL	CALE	PLLF	RT/SE	)	
	()	(i) S	SEQUE	ENCE	DESC	RIPI	rion:	SEC	, ID	NO:	50:				
ATG	CGA	CNN	TTT	TGG	TTT	CTC	ATG	TAC	CCC	TTT	CGC	TTC	CAT	GAC	TGC
Met	Arg	Xaa	Phe	Trp -40	Phe	Leu	Met	Tyr	Pro -35	Phe	Arg	Phe	His	Asp -30	Суз
AAA	CAG	AAA	TAT	GAC	CTG	TAC	ATC	AGC	ATT	GCT	GGC	TGG	CTG	ATC	ATC
Lys	Gln	Lys	Tyr	Asp	Leu	Tyr	Ile	Ser	Ile	Ala	Gly	Trp	Leu	Ile	Ile
_		-	-25	_		_		-20			_		-15		

TGC CTT GCC TGT GTA CTC TTT CCA CTC CTC AGA ACC AGT GAT GAT ACC

Cys Leu Ala Cys Val Leu Phe Pro Leu Leu Arg Thr Ser Asp Asp Thr -5

CCT GGC AAT AGG ACC AAA TGC TTT GTG GAT CTT CCT ACC AGG AAT GTC

Pro Gly Asn Arg Thr Lys Cys Phe Val Asp Leu Pro Thr Arg Asn Val

AAC CTG GCC CAG TCC GTT GTT ATG ATG ACC ATT GGC GAG TTG ATT GGG

Asn Leu Ala Gin Ser Val Val Met Met Thr Ile Gly Glu Leu Ile Gly

30

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 193 base pairs

(B) TYPE: NUCLEIC ACID

- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 2..52
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7

seq CCLFTCFFIPCIS/CK

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:
- C ATG GTT TCC TTA TGT TGT CTT TTC ACT TGT TTC TTT ATT CCT TGT ATT 49 Met Val Ser Leu Cys Cys Leu Phe Thr Cys Phe Phe Ile Pro Cys Ile
- TCC TGT AAG CTA GAA ATG TGG GGA CTC GAT GAG CCT AAA GTT AAA CCA Ser Cys Lys Leu Glu Met Trp Gly Leu Asp Glu Pro Lys Val Lys Pro

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(C) STRANDEDNESS: DOUBLE
(D) TOPOLOGY: LINEAR

(F) TISSUE TYPE: Placenta

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 57..137

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 6.9

seq ILLLVTYSPIAYS/HS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

AGCAGGCAGC CTGTGCCTTT TCTCCAAACG AAGACAGCAC TTTGAAAATT CTTTCA ATG 59 Met

GAT TTT TTT CTT GAA AGA TCG TAC TGG GGG AAA ATG ATA CTT CTA

Asp Phe Phe Phe Leu Glu Arg Ser Tyr Trp Gly Lys Met Ile Leu Leu

-23 -20 -15

TTA GTT ACA TAT TCT CCA ATC GCA TAC TCG CAC TCC CGG

Leu Val Thr Tyr Ser Pro Ile Ala Tyr Ser His Ser Arg

-10 -5 1

(2) INFORMATION FOR SEQ ID NO: 53:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 334 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F)	TISSUE	TYPE:	Lymph	ganglia
-----	--------	-------	-------	---------

lix'	l EED	THE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 170..247
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.9

seq LWVLLLCAHVVTL/LV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

ATTTTTCCTG TGGTGGGTTC ACACGCAGCT AGACACAGCT AACTTGAGTC TTGGAGCTCC	60
TAGAGGGAAG CTTCTGGAAA GGAAGGCTCT TCAGGACCTC TTAGGAGCCA GAGAAGAGGA	120
CGTTGTCACA GATAAAGAGC CAGGCTCACC AGCTCCTGAC GCATGCATC ATG ACC ATG Met Thr Met -25	178
AGA CAC AAC TGG ACA CCA GAC CTC AGC CCT TTG TGG GTC CTG CTC CTG Arg His Asn Trp Thr Pro Asp Leu Ser Pro Leu Trp Val Leu Leu Leu -20 -15 -10	226
TGT GCC CAC GTC GTC ACT CTC CTG GTC AGA GCC ACA CCT GTC TCG CAG Cys Ala His Val Val Thr Leu Leu Val Arg Ala Thr Pro Val Ser Gln -5	274
ACC AYC ACA GCT GCS ACT GCC TCA GTT AGA AGC ACA AAG GAC CCC TGC Thr Xaa Thr Ala Ala Thr Ala Ser Val Arg Ser Thr Lys Asp Pro Cys 10 20 25	322
CCC ACC CAG GGG Pro Thr Gln Gly	334

# (2) INFORMATION FOR SEQ ID NO: 54:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 254 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 78..221
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.8

seq ILRMLLSLQPVLQ/DA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

ATAGCAATTG GGTACGTGTT GAAGAGCGTG ACTGTTGCAA TGACTGCTAC CTTGCATTAG	60
AACATGGGCG TCAGTTC ATG GAT AAC ATG TCA GGA GGA AAA GTT GAT GAA Met Asp Asn Met Ser Gly Gly Lys Val Asp Glu -45 -40	110
GCA CTT GTG AAA AGT TCA TGC TTA CAC CCC TGG TCC AAA AGA AAC GAT Ala Leu Val Lys Ser Ser Cys Leu His Pro Trp Ser Lys Arg Asn Asp -35 -30 -25	158
GTG AGT ATG CAG TGC TCA CAG GAT ATA CTT CGA ATG CTC CTC TCT CTT Val Ser Met Gln Cys Ser Gln Asp Ile Leu Arg Met Leu Leu Ser Leu -20 -15	206
CAG CCA GTT CTT CAG GAT GCC ATT CAG AAA AAA AGA ACA GTA AGA CAG Gln Pro Val Leu Gln Asp Ala Ile Gln Lys Lys Arg Thr Val Arg Gln -5 1 5 10	254
(2) INFORMATION FOR SEQ ID NO: 55:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 181 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	: •
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Lymph ganglia</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 5139     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 6.7</pre>	
(%i) SEQUENCE DESCRIPTION: SEQ ID NO: 55:	
AAGG ATG YGA CTG CAA GGC CAG GAA GCT ACA GGG AAA GTT CTG ATC AAA Met Xaa Leu Gln Gly Gln Glu Ala Thr Gly Lys Val Leu Ile Lys -45 -35	49
ATA CAC AAA GAC ACA AGC CAG GTC CCC ACC GCG CKW GGC GAT GCA TCC Ile His Lys Asp Thr Ser Gln Val Pro Thr Ala Xaa Gly Asp Ala Ser -30 -25 -20	97
ATA GCA GCC TTG GTG CTG TGG ACA CTC CCT GGG GCC CAG CGA AGG GGA  Ile Ala Ala Leu Val Leu Trp Thr Leu Pro Gly Ala Gln Arg Arg Gly  -10  -5  1	145
GAG TTT GCT CCC AAA GGC GCA CCA ATG ACC AAC AGG Glu Phe Ala Pro Lys Gly Ala Pro Met Thr Asn Arg 5 10	181

- Mad - St Start	. <del></del>
WO 99/06	553 PCT/IB98/012
(2) INFORM	ATION FOR SEQ ID NO: 56:
(i)	SEQUENCE CHARACTERISTICS:
(=/	(A) LENGTH: 108 base pairs
	(B) TYPE: NUCLEIC ACID
	(C) STRANDEDNESS: DOUBLE
	(D) TOPOLOGY: LINEAR
(ii)	MOLECULE TYPE: CDNA
(vi)	ORIGINAL SOURCE:
	(A) ORGANISM: Homo Sapiens
	(F) TISSUE TYPE: Lymph ganglia
(ix)	FEATURE:
	(A) NAME/KEY: sig_peptide
	(B) LOCATION: 2296
	(C) IDENTIFICATION METHOD: Von Heijne matrix
	(D) OTHER INFORMATION: score 6.6 seq ILVLILFPTSCVM/QV
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 56:
: AACCTACACA	ATGATAGTGT A ATG ACT GAG CAC TCA CTG ACG CAT CAA GGG 51

Met Thr Glu His Ser Leu Thr His Gln Gly -25 -20 ATC CCA ATT CTA GTC TTG ATT CTA TTT CCA ACT AGT TGT GTC ATG CAA Ile Pro Ile Leu Val Leu Ile Leu Phe Pro Thr Ser Cys Val Met Gln -15 108 GTC CTC TGG Val Leu Trp

- (2) INFORMATION FOR SEQ ID NO: 57:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 213 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: 118..174
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.5 seq RFIFLTSLQLISS/SY
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

AAATCTTGAA GTGTATTGTT GAATCATAGA TGTTTTTATG TGGCTATCTA TTCCTTACTT

AATCCTTCAT TTTCAAGAAG ATTGTGTCGT WAAAGCCCTT AAAATTTGGT ACCCTTT	117
ATG TAC ATT GGT GGT CTG AGA TTC ATT TTT CTC ACC TCT TTA CAA CTA Met Tyr Ile Gly Gly Leu Arg Phe Ile Phe Leu Thr Ser Leu Gln Leu -15 -10 -5	165
ATT TCA AGC AGC TAT GTT ACC ACT TTA TTA AAA AAA AAC ACA CTT AGG Ile Ser Ser Tyr Val Thr Thr Leu Leu Lys Lys Asn Thr Leu Arg 1 5 10	213
(2) INFORMATION FOR SEQ ID NO: 58:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 227 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Lymph ganglia</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 105218     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 6.5</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:	
ATGATTAAAG AAATGATCTT TTAAAGCAAA ATTGTTTGCT GTAGCCAGTG ACAGCTTATT	60
TAAAGAAAGT GTTTAACTTA TTTGATTTTA GCATGTTTTA GTAA ATG TCT GTT AGT Met Ser Val Ser -35	116
CTT AAA CAC ATT CAC TTG CAT TTT ATT ATT ATG TCG GTA CTT GTA TTT Leu Lys His Ile His Leu His Phe Ile Ile Met Ser Val Leu Val Phe -30 -25 -20	164
TGG AAC TGT AGT CAT TTG ATT TTC TTT TCC TTG ATT TTT TTA AAC CTG Trp Asn Cys Ser His Leu Ile Phe Phe Ser Leu Ile Phe Leu Asn Leu -15 -5	212
TTT GCG ATC TCC TGG Phe Ala Ile Ser Trp 1	227

WO 99/06553	44 PCT	/IB98/012
(A) (B) (C)	NCE CHARACTERISTICS: LENGTH: 186 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLEC	CULE TYPE: CDNA	
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Lymph ganglia	
(B) (C)	URE:  NAME/KEY: sig_peptide  LOCATION: 106171  IDENTIFICATION METHOD: Von Heijne matrix  OTHER INFORMATION: score 6.3  seq MVSFLSXPFLCSA/KP	
(xi) SEQUI	ENCE DESCRIPTION: SEQ ID NO: 59:	
AAGCYCMGNY ATCC	TTGGAA ATAACCTCAA AARGCCTTAG GCTAATGCAC AGGGTTCTTC	60
CTTCTAGTTC TGAC	TCACCT TCCTGACCTC ATTTTATGCC TCACT ATG ARD ASA CTT  Met Xaa Xaa Leu -20	117
	TTT ATG GTC TCT TTC CTA TCA MWC CCC TTT CTT TGT Phe Met Val Ser Phe Leu Ser Xaa Pro Phe Leu Cys -10 -5	165
TCA GCA AAA CCA Ser Ala Lys Pro 1		186
(2) INFORMATION	FOR SEQ ID NO: 60:	
- (A) (B) (C)	NCE CHARACTERISTICS: LENGTH: 267 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLE	CULE TYPE: CDNA	
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Lymph ganglia	
(ix) FEAT	'URE:	

(A) NAME/KEY: sig\_peptide (B) LOCATION: 55..111

(D) OTHER INFORMATION: score 6.3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

(C) IDENTIFICATION METHOD: Von Heijne matrix

seq ILVSVAAATGAHS/QL

ACC	CAHN	AC (	CACAC	CCCI	rc ci	TGG	SAGA	A TC	CCT	GAT	CAC	AGCT	CCT (	CACC	ATG Met	57
	TGG Trp															105
	TCC Ser															153
	GCC Ala															201
	CGT Arg															249
	ATG Met									f					·	267
(2)	INFO	; ORMA:	rion	FOR	SEQ	ID t	NO: (	51:						:		
(2) INFORMATION FOR SEQ ID NO: 61:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 259 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR																
	(:	ii) 8	MOLE	CULE	TYPE	E: CI	ONA									
	(1	vi) (		INAL ORGA TISS	ANIS	1: Ho		-		lia						
	<u>(</u> :		(C)		ATION NTIF:	N: 9: ICAT:	2 2: ION 1	26 Metho	OD: 1	re 6	_					
	(	xi) [	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	61:		_	٠		
AAA	GCAG	YST	ACCT	TGTA	TG G	GCAG	TGGA	G CA	AGCT	AAGG	AGA	CACA	GGA	GATA	TATGGG	60
AAC	CTAA	AGT	GGAA	TTTT	CA A	ATTC	TTGC				TCA Ser		Phe			112
				Val					Leu					Pro	ATT Ile	160

AAC CCA TCC CCA AAC AGT GCC ATT NNG GTA GCT TGT GTG CTC TCT TCT

Asn	Pro	Ser -20	Pro	Asn	Ser	Ala	Ile -15	Xaa	Val	Ala	Cys	Val -10	Leu	Ser	Ser	
CTT Leu	ATT Ile -5	GCT Ala	GTT Val	AAC Asn	TCA Ser	GCT Ala 1	CAC His	CCA Pro	GAA Glu	AGT Ser 5	ACT Thr	ATT Ile	GAC Asp	ACC Thr	CGC Arg 10	256
TGG Trp					-		-									259
(2)	INFO	ORMA!	rion	FOR	SEQ	ID 1	NO: (	62:								
	( i	L) SI	(A) (B) (C)	LENG TYPE STRA	STH: E: NU ANDEL	165 JCLEI DNESS	RISTI base (C AC S: DC (NEAF	e pai CID OUBLE						·		
	ίĵ	Li) N	OLE	CULE	TYPE	E: CI	ONA									
	(1	/i) (	(A)	ORGA		1: Hc	omo S : Umb	-		cord		:				
	: :	Lx) I	(B) (C)	NAME LOCA IDEN	TION TIF	I: 76	ig_pe 515 ION N MATIC	59 ÆTHO	D: V	on ice 6.	. 3 ¯					
	(3	(i) S	SEQUI	ENCE	DESC	CRIP!	rion:	: SE(	Q ID	NO:	62:					
AGAT	GTC	CAT A	AATT	attg(	GT A	ACTC	AGTT	A CC	TTCT	AACT	AAT	AGGC:	rgg '	rtcad	GGAGAC	: 60
TCT(	CCA(	GTT '	TATA					u Gl					Cy:		T AAA e Lys	111
							ATT Ile								GGC Gly	159
	GGG Gly							-								165
(2)	INF	ORMA	TION	FOR	SEQ	ID	NO:	63:								
		i) S	EQUE (A) (B) (C)	NCE LEN TYP: STR	CHAR GTH: E: N ANDE	ACTE 388 UCLE DNES	RIST bas IC A S: D INEA	ICS: e pa CID OUBL			-					

(ii) MOLECULE TYPE: CDNA

WO 99/06	553			47		·	/1D76/U
(vi)		SOURCE: ANISM: Ho	_				
(ix)	(B) LOC (C) IDE	E/KEY: si ATION: 74	I178 CON METHO	DD: Von H	leijne mat 3 LLSPGXSGS		•
(xi)	SEQUENCE	DESCRIPT	CION: SE	Q ID NO:	63:	41	
AACTTAACAT	GCCGCCGC	CG GCGCA	CTGCC GA	GCCCCTG	AGCGGGTCG	C GAGCGTGGTG	60
TTACACTCCA			Arg Gln A		GGC AGC GG Gly Ser Gl		109
GAG ACA TG Glu Thr Cy					Leu Lys L		157
AGC CCG GG Ser Pro Gl							205
GTC TTG TT Val Leu Le 10							253
		Gln Trp				GA GAT GAA rg Asp Glu 40	301
		a Glu Trp		Asn Ser		TC ACT TGG al Thr Trp 55	349
AGT TTT AC Ser Phe Th							388
		- <b></b>					

# (2) INFORMATION FOR SEQ ID NO: 64:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 282 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia

<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 118174     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 6.2</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:	
ATTGTAAYAA AAATATTTAC TACTCTTACT GGACTTAGTT TCCTTTTTGT GGTTTCTGTT	60
ACGTGGTCTA TAAGTTTCAA GCAGTGAGCT TAATTTGTGC GTCATAAAAA TTTGGTT	117
ATG AGT ACA CAG AAG GGA CTT GCT CTG TTT CTC ATG GCC CTT GGC TTT Met Ser Thr Gln Lys Gly Leu Ala Leu Phe Leu Met Ala Leu Gly Phe -15 -5	165
TCA TGC ATA CAC AAG AAG TTT CAG GAG TCA GAG GAG GGT AAG CAC CAT Ser Cys Ile His Lys Lys Phe Gln Glu Ser Glu Glu Gly Lys His His 1 5 10	213
ATG GGT GGA ATT AAT AGG TCT CAT TGG GTT AAG TCT CGA AAG AGC TGT Met Gly Gly Ile Asn Arg Ser His Trp Val Lys Ser Arg Lys Ser Cys 15 20 25	261
TTA ATA AAT AGC CAA CGC AAG Leu Ile Asn Ser Gln Arg Lys 30 35	282
(2) INFORMATION FOR SEQ ID NO: 65:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 147 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE:	
(A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Lymph ganglia	,
(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 67141  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 6.1  seq YFLIVFFVFLCNC/HQ	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:	
ACAGACATTT CATACTGGCC ATCTTGATGT AGATTACATT GCCATCCTGT GTCCTGATTG	60
TACTTT ATG AAA GAT GTA GAA ATA ATC ATG ATA TTT CAC GGT TAT TTC  Met Lys Asp Val Glu Ile Ile Met Ile Phe His Gly Tyr Phe  -25	10

TTG ATT GTG TTT TTT GTG TTC CTA TGC AAC TGC CAC CAG Leu Ile Val Phe Phe Val Phe Leu Cys Asn Cys His Gln -10 -5 1	147
(2) INFORMATION FOR SEQ ID NO: 66:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 345 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Lymph ganglia</pre>	
(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 214339  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 6.1  seq AILLLQSQCAYWA/LP	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:	
AARTTGAGCT TGGGGACTGC AGCTGTGGGG AGATTTCAGT GCATTGCCTC CCCTGGGTGC	60
TCTTCATCTT GGATTTGAAA GTTGAGAGCA GCATGTTTTG CCCACTGAAA CTCATCCTGS	120
TGRSAGTGTA MTGGATTATT CCTTGGGCCT GAATGACTTG AATGTTTCCC CGCCTGAGCT	180
AACAGTCCAT GTGGGTGATT CAGCTCTGAT GGG ATG TGT TTT CCA GAG CAC AGA Met Cys Phe Pro Glu His Arg -40	234
AGA CAA ATG TAT ATT CAA GAT AGA CTG GAC TCT GTC ACC AGG AGA GCA Arg Gln Met Tyr Ile Gln Asp Arg Leu Asp Ser Val Thr Arg Arg Ala -35 -20 -20	282
CGC CAA GGA CGA ATA TGT GCT ATA CTA TTA CTC CAA TCT CAG TGT GCC Arg Gln Gly Arg Ile Cys Ala Ile Leu Leu Gln Ser Gln Cys Ala -15 -5	330
TAT TGG GCG CTT CCA	345

# (2) INFORMATION FOR SEQ ID NO: 67:

1

Tyr Trp Ala Leu Pro

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 253 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE

THE THE THE

(D) T	OPOLOGY:	LINEAR
-------	----------	--------

- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 155..223
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.1

seg SSILSTFVSWLSA/FY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

AATATAATTT GATATATAAA TATACTTCCC CACGCAATTA ATAAGCAAGT GCTGGAGAGA 60

CATTITAAGA TICTGTAAAT ATCCTGCTGC ACATGAAAAG TITCCCCCTA GATTGAGCGT 120

CTGCTGATGA TTCTTGTGTG ATCCAGCATT TACT ATG TTG GTT GTA AAA CAA TGC 175

Met Leu Val Val Lys Gln Cys
-20

TTT TCT GAC TCC AGT ATT CTC TCC ACA TTC GTA AGT TGG CTC TCA GCA

Phe Ser Asp Ser Ser Ile Leu Ser Thr Phe Val Ser Trp Leu Ser Ala

-15

-10

-5

TTC TAC TGT AAA GAA GGA CCC TCC TCG GGG
Phe Tyr Cys Lys Glu Gly Pro Ser Ser Gly
1 5 10

253

#### (2) INFORMATION FOR SEQ ID NO: 68:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 350 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 39..134
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.1
    - seq LPLLTSALHGLQQ/QH
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

Met Ile Xaa Leu Arg Asp -30

					CTT Leu -20							104
	Thr				GGA Gly						;	152
					AAG Lys							200
					AGC Ser						:	248
Leu					ACC Thr 45						;	296
					GTA Val							344
	GGG Gly		,	•			:			•		350

#### (2) INFORMATION FOR SEQ ID NO: 69:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 315 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 265..306
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.9

seq ITMMLALISVCLF/AF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

AUTAATTIGA AGTCATACCA GCTTGAGTTA GATAACATAC AAAATTCTGT TCCTTTTCA 60
UTTGTTGATG TAACAAAATT ACATCTTTAT ACATTGTGTA CACAACAACA TAAGCTAATA 120
ATTTAATACA CTCATTTCTT AAATTGTAGA AAACAAAATT GGGCTTACCA ATCAAATTAC 180

· water

AATAATATGA GATTTTAAAT TTGTAATTTA AAAAAATATT AGTTTCTTAA ATCATGTAGA 240

AAACAAAAAG TAAAGTCACA CATC ATG ATT ACA ATG ATG TTA GCT CTT ATA

Met Ile Thr Met Met Leu Ala Leu Ile -10	
AGT GTC TGC CTA TTT GCV TTT TGG Ser Val Cys Leu Phe Ala Phe Trp -5 1	315
(2) INFORMATION FOR SEQ ID NO: 70:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 346 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
(vi) ORIGINAL SOURCE:  (A) ORGANISM: Homo Sapiens  (F) TISSUE TYPE: Umbilical cord	
(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 191235  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 5.9  seq LLTLVQCSDLCPS/CS	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:	
ACTGACATTG RTTATCCARA ATGACTAACA CTCTTCTACA TTAAATAGGG AAAGAGCCTG	60
ATTACAGTCC CTCCAACAGT CTACACAAAT ACCCCCCAAC ACACACRTAT RATTGAGGGT	120
GAAGTGTTTT CTAGATCATT GCCTAAGTCC CCCATTTGCT TTCAGAATAG ACCCAGGCRR	180
GTAAAAGGGA ATG TGG CTC TTA ACA CTA GTT CAA TGT TCT GAC CTK TGT  Met Trp Leu Leu Thr Leu Val Gln Cys Ser Asp Leu Cys  -15 -10 -5	229
CCT TCC TGC TCC CAA GCA TTG ACA CTT GTG TTA GTA TCT TTT TCT GAA Pro Ser Cys Ser Gln Ala Leu Thr Leu Val Leu Val Ser Phe Ser Glu  1 5 10	277
GTC AGA GAC TTG GCA GAG ACC TCC CTA TCA TCT AAT CTG AAG AAC TCT Val Arg Asp Leu Ala Glu Thr Ser Leu Ser Ser Asn Leu Lys Asn Ser 15	325
TTG TTT ATA GTT CTG AAG AGG Leu Phe Ile Val Leu Lys Arg 35	346

V	VO 99/06553	53	PCT/1B98/0
(2)	INFORMATION	FOR SEQ ID NO: 71:	
	(A) (B) (C)	NCE CHARACTERISTICS: LENGTH: 179 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
	(ii) MOLE	CULE TYPE: CDNA	
	(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Lymph ganglia	
	(B) (C)	URE:  NAME/KEY: sig_peptide  LOCATION: 27119  IDENTIFICATION METHOD: Von Heijne matrix  OTHER INFORMATION: score 5.9  seq LLFACLTMLLVKT/CQ	
	(xi) SEQU	DENCE DESCRIPTION: SEQ ID NO: 71:	
ATTA	ACCAGTG TACA	ACTTGAG AGAGCT ATG AGA GTA CAT CTT TTC CCA TAC CT Met Arg Val His Leu Phe Pro Tyr Le -30 -25	eu 53
TGT Cys	CAA CCT AGT Gln Pro Sex -20	r GTA CTA TCA AAC TTT TTG TTA TTT GCT TGT CTT ACT r Val Leu Ser Asn Phe Leu Leu Phe Ala Cys Leu Thi -15 -10	101
ATG Met	TTG TTG GTG Leu Leu Val	G AAA ACG TGT CAG GAG TCC CCA AAA TCA CCC CTA AG 1 Lys Thr Cys Gln Glu Ser Pro Lys Ser Pro Leu Ser 1 5	c
	Met Ile Cys	C CAG ACT TAT AGA ATT GGG s Gln Thr Tyr Arg Ile Gly 15 20	179
(2)	- INFORMATION	N FOR SEQ ID NO: 72:	
		ENCE CHARACTERISTICS: ) LENGTH: 261 base pairs	· -

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 121..165
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.7

#### seq PLCFLILPYPVLS/SH

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

ATTTYGGG	STC T	ACGC	ATTC	T GC	TACI	'ACTC	стс	STTTI	CCT	CTAC	CAACO	STC (	CCATO	TTTAT	60
CCTAGTGA	ATG T	GTCC'	TACT	T AC	AACA	TATA	TAC	CTCCF	ATCT	CCAC	CCT	CAG (	CAGCO	CTGTC	120
ATG ATT Met Ile -15															168
CAT GAC His Asp															216
ATT AAC Ile Asn															261

#### (2) INFORMATION FOR SEQ ID NO: 73:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 144 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 28..123
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.5 seq CLLSXPSTRKSQA/CM
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:
- ACCTGCTCTA GCGGGCCGCG TAGACCA ATG GCG GGC TCC CGG CTC CCG CGG CAG

  Met Ala Gly Ser Arg Leu Pro Arg Gln

  -30 -25
- CTC TTC CTC CAG GGC GTG SMG GCG TCT TCA TGT TTG CTT TCR MTT CCC 102
  Leu Phe Leu Gln Gly Val Xaa Ala Ser Ser Cys Leu Leu Ser Xaa Pro
  -20 -15 -10
- TCT ACA CGC AAA TCC CAG GCC TGT ATG GCC CCG AGG GCA TGG

  Ser Thr Arg Lys Ser Gln Ala Cys Met Ala Pro Arg Ala Trp

  -5

  1

  5

-

121	INFORMATION	FOR	SEO	TD	NO:	74:
(2)	TREOUTHTON	101	222			

- <b>-</b> -		
(i)	SEQUENCE	CHARACTERISTICS:

- (A) LENGTH: 250 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

# (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 146..229
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.4

seq FVLHLLAQDLVCC/FY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

ATGGCCTTTA TTTCTGTTCT TACTCCAACA TTTTCTCATC TTTTCTCCCA TCCTTTACT

120

ATTCAATTAA TATATTTCTC TGTAT ATG TAT ATA TGC TTT TGT TTG GAA TCA

Met Tyr Ile Cys Phe Cys Leu Glu Ser

-25

TTT GAA ATT AAG TGT GGA TTT GTT CTC CAT CTT CTT GCT CAG GAT TTG

Phe Glu Ile Lys Cys Gly Phe Val Leu His Leu Leu Ala Gln Asp Leu

-15

-10

-5

GTG TGC TGC TTT TAT CTG AGG ACA TNN BAR
Val Cys Cys Phe Tyr Leu Arg Thr Xaa Xaa

1 5

250

# (2) INFORMATION FOR SEQ ID NO: 75:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 231 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 127..186
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.4

#### seq LNAFTLLVWLSLS/KN

(xi)	SECUENCE	DESCRIPTION:	SEO	ID NO:	75:

ATTTTAATAT	AATGCATTAA AATGTCAGGT A	ATACTGTAT ATTCTATATT	GCATCACAAC 60
AGGAGATATA	TCTGGATGAC CTACCATTAG TO	GATGCTAAG TTTTACÁTTG	TATTGGAGCA 120
	CAT TTC ATC CTC CAT AAC His Phe Ile Leu His Asn -15	•	
	A TCT CTT TCT AAA AAT AC 1 Ser Leu Ser Lys Asn Th		•
GCA TCG GC. Ala Ser Al			231

#### (2) INFORMATION FOR SEQ ID NO: 76:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 194 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 84..188
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.2

seq IAPLFTLLPKSIP/AP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

ACACTCATTC TATACTGGGC ACCATGTCTG ATCATTTTTT TTTCTGATAT TTGGATCAGT 60

TCTATTAAAC TGATAACCCT GTG ATG TCT TTT TTT CCC TTC AAT AGA TCT TTA 113

Met Ser Phe Phe Pro Phe Asn Arg Ser Leu

-35

-30

AAT TCC AAT CCT CAC CCT AAT CTA CTC TTT CCC AAT ATA GCA CCG TTA

Asn Ser Asn Pro His Pro Asn Leu Leu Phe Pro Asn Ile Ala Pro Leu

-25 -10 -10

TTC ACA CTG CTC CCA AAA TCT ATT CCA GCC CCG
Phe Thr Leu Leu Pro Lys Ser Ile Pro Ala Pro

-5 1

		•.														
(2)	INFC	RMAT	ION	FOR	SEQ	ID N	10: 7	7:								
	(i	.) SE	(A) (B) (C)	LENG TYPE STRA	TH: : NU NDED	169 CLEI NESS	DASE C AC : DO NEAR	pai ID UBLE				٠				
	(i	.i) M	OLEC	ULE	TYPE	: CE	NA									
	(v	/i) O	(A)	ORGA	NISM	: Ho	mo S Umb			ord						
	<b>(i</b>	.x) F	(A) (B) (C)	NAME LOCA IDEN	TION TIFI	: 8. CATI		ETHO	D: V scor	e 5.	leijn 2 HCFC					
	()	(i) S	EQUE	NCE	DESC	RIPT	ION:	SEÇ	Q ID	NO:	77:					
														:		
AAAC	AGA	ATG Met									TTT Phe					49
CAT His	TGC Cys	TTT Phe	TGC Cys	AGC Ser -5	CTT Leu	GCA Ala	AAG Lys	ACA Thr	AAA Lys 1	AAT Asn	GGT Gly	TTA Leu	AGT Ser 5	TGG Trp	GGA Gly	97
		CAA Gln 10														145
		TTT Phe					Leu	,								169
(2)		ORMA														
							base		irs							

- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 223..294

<ul><li>(C) IDENTIFICATION METHOD: Von Heijne matrix</li><li>(D) OTHER INFORMATION: score 5.2</li><li>seq PGLCCPALGSAWS/KN</li></ul>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:	
ACTCCCTGAA CCCTAACTCA CCCTTTGCCC TCCCCACCCT TCAGCCCCTG CCCAGGTCTT	60
GGAGATCTCT GTGCTGTCTT TTGTGGAGCA GCTGCTATCT TGCAGTCAGA TCCTCTGTCG	120
GGGAGGCCTT CAGCTTTTGT TCAACGACCC AGAGGGTGTG GGAGGGGCTC AGTTACTCTT	180
CTCCTCACCT GGCACTTAGA GAAAGCAAGT CTCAAGAGTC TC ATG GTA TGT GGT Met Val Cys Gly	234
TGG TGG ACC CAG GGG CCT GTG CCC GGT CTG TGC TGT CCA GCT TTG GGC Trp Trp Thr Gln Gly Pro Val Pro Gly Leu Cys Cys Pro Ala Leu Gly -20 -15 -10 -5	282
TCT GCC TGG AGC AAA AAC AAG AGC NTG CCT GTG CCG TGT TGC GGT CCT Ser Ala Trp Ser Lys Asn Lys Ser Xaa Pro Val Pro Cys Cys Gly Pro 1 5 10	330
TAC ATG GTA GCG AAT CTC GGG Tyr Met Val Ala Asn Leu Gly 15	351
13	:
(2) INFORMATION FOR SEQ ID NO: 79:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 362 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Lymph ganglia</li></ul>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 231308     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 5.2     seq FECALVSASLTTA/GT</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:	
AATTTTCAAA AGTGCTGTTA ACATAAACAG AGCAGTAAAT CTGGGGCACC ATGCTTTTTT	60
TTCAAAGTTG TTAAGAATTA TATCAGTCTG CAGGTGTCAC ACGCAGTTAC TCAGRATCAG	120
AWAGAAGGCT GATCGGGGGT TAGATCTCCA TCTATCTATC TTTTTGCAAC CAACCACGTC	180

CAGGCTGTTT ATTTAATACT TCCTCTTGCT AATGAAGGTA CTGGTTGGGG ATG GGT

· was the same

Met Gly -25

CGA GCT TTC CCA TCT CGG CAT AAG ACT GCA AGA TTT GAA TGT GCC CTG
Arg Ala Phe Pro Ser Arg His Lys Thr Ala Arg Phe Glu Cys Ala Leu
-20

GTG TCG GCT TCA CTG ACC ACA GCA GGT ACC CCA GGC AAG AAT CTK WGC
Val Ser Ala Ser Leu Thr Thr Ala Gly Thr Pro Gly Lys Asn Leu Xaa
-5

AGT TAT AAC AGT GCG GAG GCA AGA CAC ATC
Ser Tyr Asn Ser Ala Glu Ala Arg His Ile
10

284

AGA TTT GAA TGT GCC CTG
ACC CTG
ACC CTG
ACC ATC
STR AAG AGT GCG GAG GCA AGA CAC ATC
STR TAT AAC AGT GCG GAG GCA AGA CAC ATC
STR TAT AAC AGT GCG GAG GCA AGA CAC ATC
STR TAT AAC AGT GCG GAG GCA AGA CAC ATC
STR TAT AAC AGT GCG GAG GCA AGA CAC ATC
STR TAT AAC AGT GCG GAG GCA AGA CAC ATC

#### (2) INFORMATION FOR SEQ ID NO: 80:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 218 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Placenta
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 150..203
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5

seq LCXXLLCVLFVSH/FY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

AATYTGAATT GAAAATTAGC TTCATGTTGT TAAGATGATC ATATCACCTG AGAGAGTTCC 60

CAAGTCYACA ATTGCTCTAC TAGTTACTAT TCAGTGTTTG TSAAAAATHT TAATCTCAGT 120

ACTGTGAAGA AGCTGGAAAA AGGGATATT ATG GGG CTA AAA GCT CTC TGT TTS

Met Gly Leu Lys Ala Leu Cys Xaa

-15

SGG CTG CTT TGT GTT CTT TTT GTC TCT CAT TTT TAC ACA CCC ACT

Xaa Leu Leu Cys Val Leu Phe Val Ser His Phe Tyr Thr Pro Thr
-10 -5 1 5

- (2) INFORMATION FOR SEQ ID NO: 81:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 363 base pairs
    - (3) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE

(D)	TOPOLOGY:	LINEAR
-----	-----------	--------

# (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens(F) TISSUE TYPE: Lymph ganglia

# (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

- (B) LOCATION: 82..309
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5

seq FPLLALLFEKCEQ/ST

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

AAGTGTGATG AAGATTGGCA CCCAGACACC ATTCGCTTTT CACCCAAGAT GATTTGATGT	60
CTTATAAAAC TCTGATGAAC C ATG ATG GCT ACA CAG ACA TTA AGT ATA GAC  Met Met Ala Thr Gln Thr Leu Ser Ile Asp  -75  -70	111
AGC TAT CAA GAT GGG CAA CAG ATG CAA GTA GTA ACA GAG TTA AAG ACA Ser Tyr Gln Asp Gly Gln Gln Met Gln Val Val Thr Glu Leu Lys Thr -65 -55	159
GAA CAA GAT CCA AAC TGC TCT GAA CCC GAT GCA GAA GGA GTG AGC CCT Glu Gln Asp Pro Asn Cys Ser Glu Pro Asp Ala Glu Gly Val Ser Pro -50 -45 -35	207
CCC CCT GTG GAG TCT CAG ACC CCG ATG GAT GTG GAC AAG CAG GCC ATT Pro Pro Val Glu Ser Gln Thr Pro Met Asp Val Asp Lys Gln Ala Ile -30 -25 -20	255
TAT AGG CAT CCA CTA TTT CCA TTA TTA GCT TTG TTG TTT GAA AAA TGT Tyr Arg His Pro Leu Phe Pro Leu Leu Ala Leu Leu Phe Glu Lys Cys -15 -10 -5	303
GAA CAA TCT ACA CAG GGC TCT GAA GGC ACA ACT TCT GCC AGT TTT GAT Glu Gln Ser Thr Gln Gly Ser Glu Gly Thr Thr Ser Ala Ser Phe Asp  1 5 10	351
GTA GAC ATC GGG Val Asp Ile Gly	363

#### (2) INFORMATION FOR SEQ ID NO: 82:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 258 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:

-25

W C 33/00222	61	
	) ORGANISM: Homo Sapiens ) TISSUE TYPE: Umbilical cord	
(B (C	TURE: ) NAME/KEY: sig_peptide ) LOCATION: 163225 ) IDENTIFICATION METHOD: Von Heijne matrix ) OTHER INFORMATION: score 4.9 seq SVFLSGSVCLSFL/SE	
(xi) SEQ	UENCE DESCRIPTION: SEQ ID NO: 82:	
ATGAGGTTTT AGT	TCTTTGG GCAGTAGCAA GTAGTGATAG GTGATGGTGG TCTGTGGTTC	60
ATGGACCAAA AAA	TGTTTGA GAGGCATGGA GGATCTTTAG ACAAGATCAC CTTCTAGGTG	120
TATGTGGTAG CAT	TCTGTTC CACCGCTCTC TTCTCCTTCA GG ATG TCT CCC TCC  Met Ser Pro Ser  -20	174
CAG CTA ACC TG Gln Leu Thr Cy -15	SC TCG GTG TTC CTC AGT GGG AGC GTT TGC CTT AGC TTT  VS Ser Val Phe Leu Ser Gly Ser Val Cys Leu Ser Phe  -10 -5	222
	AT CGT ACT TAC TTT TTC TGC CCA CTG Ls Arg Thr Tyr Phe Phe Cys Pro Leu 5 10	258
(i) SEQU (A (E	DN FOR SEQ ID NO: 83:  UENCE CHARACTERISTICS: A) LENGTH: 132 base pairs B) TYPE: NUCLEIC ACID C) STRANDEDNESS: DOUBLE D) TOPOLOGY: LINEAR	
(ii) MOI	LECULE TYPE: CDNA	
(P	IGINAL SOURCE: A) ORGANISM: Homo Sapiens F) TISSUE TYPE: Lymph ganglia	
1) 2) 1)	ATURE: A) NAME/KEY: sig_peptide B) LOCATION: 37126 C) IDENTIFICATION METHOD: Von Heijne matrix D) OTHER INFORMATION: score 4.8	
(YI) 3E	KORKOT DECOUTITION. BRK IS NO. 44.	
AAAAACATGT CC	TGGGTTGG CAGCTTGAGA TGATAA ATG CTT CAA GCC CTA GCC Met Leu Gln Ala Leu Ala	54

-30

CCG GCA CAC CAC TTA TGC TCC CTG AAG AGG TCA TTC TGT TCT CTG Pro Ala His Leu Cys Ser Leu Lys Arg Ser Phe Cys Ser Leu Leu

-20	<del>-</del> 15	-10

TGC CTT CGC ACA CAG CTC TTC CCC CAC GGG
Cys Leu Arg Thr Gln Leu Phe Pro His Gly
-5

132

# (2) INFORMATION FOR SEQ ID NO: 84:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 487 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 383..424
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.8

seq LFLKYLWRSLCRG/GI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

AGATATTTGG TGTGTCGTAG GCTTTGTTGC GAGTGGACTC TTGCATCATA TGTGGCTGTT	60
GGAGAATTGA TTCCCAGCCT TTTCGCCTGG CTGAGACCTT GTATTCCAGT TCTAGGCATC	120
ACATCCAACT CAACAGTGTC CATGGGAAAA AGAGCATCTC TTTAAAGCAA GAAAACCTTT	180
TCCAGAAGCT TCCTGCAGAC CTCCCTTCAC ACCTCGTTGA CCAGGCTGAT GGTGTGTGCC	240
AGTGCCTAAG TCAAGTCATT GACAACAGGA AGAAGATGAG CCCTGGCTGA GTTAAACTGA	300
CCAGGATGTG CATCCCCCC ATGCTGGAAG TGAGGCCGTC TTCCCTGAGA GTCAGTATCC	360
GAACAGAAAG ATCACCCAAT GC ATG TTG TTT TTA AAG TAC TTA TGG AGA TCT  Met Leu Phe Leu Lys Tyr Leu Trp Arg Ser  -10 -5	412
CTG TGC CGT GGT ATC ATC CGT ATG AAC CAT CCA GGC TGT AGT CAG Leu Cys Arg Gly Gly Ile Ile Arg Met Asn His Pro Gly Cys Ser Gln 1 5 10	460
AGA ATC AGA GAC TCG CTG TGT GAT CTC	487

20

(2) INFORMATION FOR SEQ ID NO: 85:

Arg Ile Arg Asp Ser Leu Cys Asp Leu

15

(i) SEQUENCE CHARACTERISTICS:

THAT IS THE		. <del></del> .	
WO 99/06553		63	PCT/IB98/01
(B) (C)	LENGTH: 296 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR		
(ii) MOLE	CULE TYPE: CDNA		
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Lymphocyt		•
(B) (C)	NAME/KEY: sig_peptide LOCATION: 12122 IDENTIFICATION METHOD: OTHER INFORMATION: sc		
(xi) SEQU	ENCE DESCRIPTION: SEQ	ID NO: 85:	
		CAT TCT TGG CGC TGG GCG His Ser Trp Arg Trp Ala -30	
	Phe Glu Lys Arg Arg H	AC TCC GCG ATT CTG ATC C is Ser Ala Ile Leu Ile I 15 -10	
	Val Ser Gly Ser Gly P	CG CAG TGG AGG CCA CAT ( Pro Gln Trp Arg Pro His (	
		AC CAG ATT CCA GAG TCA 'yr Gln Ile Pro Glu Ser :	
		AAA GGC AAT TCA GGA CAG ys Gly Asn Ser Gly Gln 35	
		TGG CCA CTG ATA GAA AAG Trp Pro Leu Ile Glu Lys 50 55	
ACT TGG Thr Trp			296

- (2) INFORMATION FOR SEQ ID NO: 86:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 211 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:

WO 99/06553	64 PCT//	(B98/01
(A) (F)	ORGANISM: Homo Sapiens TISSUE TYPE: Placenta	
(B) (C)	URE:  NAME/KEY: sig_peptide  LOCATION: 65178  IDENTIFICATION METHOD: Von Heijne matrix  OTHER INFORMATION: score 4.8  seq LASLFGLDQXAAG/HG	
(xi) SEQU	ENCE DESCRIPTION: SEQ ID NO: 86:	
AACGACGTCG GCGG	TGACAG GCCCGTGGGA CTYTGGGRAT ACCCAGCKTC CTCCCCGCAA	60
	C ARC GCA ATG TTC GGT GCG GGG GAC GAG GAC GAC ACC a Xaa Ala Met Phe Gly Ala Gly Asp Glu Asp Asp Thr -35 -30 -25	109
	CCG AGC GGC GGT GCC AGA TTG GCC TCA CTT TTT GGA Pro Ser Gly Gly Ala Arg Leu Ala Ser Leu Phe Gly -15 -10	157
	GCT GCT GGC CAT GGA AAT GRA TTK TTC CAG TAC ACA Ala Ala Gly His Gly Asn Xaa Xaa Phe Gln Tyr Thr 1 5	205
GCC CCA Ala Pro 10		211
(2) INFORMATION	FOR SEQ ID NO: 87:	
(A) (B) (C)	INCE CHARACTERISTICS: LENGTH: 277 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLE	ECULE TYPE: CDNA	,
(A)	GINAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Lymph ganglia	
(B) (C)	TURE:  NAME/KEY: sig_peptide  LOCATION: 215253  IDENTIFICATION METHOD: Von Heijne matrix  OTHER INFORMATION: score 4.7  seq MLWLLRSLTDVSS/MI	

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

AGCTCTTCTG AAGGTCAGGT CATCTAACTC CCTTGACCTC CTCCTTGAAG CTGTGAGCTA CTTCTTGGCG ATGCCCCTCC ATGCAGGAGA GACTTGCACT TAGCTTCCTG CTTTTCCCCT 120

CCTC	CCCA	AC . T	CCTG	CCAT	G TC	ATTT'	rtac	CCA	rttt'	IGT (	GACC'	rcag(	CA T	TGAT'	TGGT'	r :	180
GGAA	CCAC	CT A	ACGC(	CATG:	r agʻ	rtga/	ACCA	TTC			C TGG		u Le				235
TTA Leu																;	277
(2)	INFO	RMAT	ION	FOR :	SEQ	ID N	0: 8	8:									
•	<b>(</b> i		QUEN(A) : (B) : (C) : (D) : (D)	LENG' TYPE STRAI	TH: : : NUC NDEDI	206 I CLEI NESS	oase C'AC: DOI	pai: ID UBLE	rs				-				
•	(i	i) M	OLEC	ULE '	TYPE	: CD	NA										
	(v	i) O	RIGI (A) (F)	ORGA	NISM	: Ho	mo S Lym	apie ph g	ns angl	ia				٠.			
	(i	ж) F	(A) (B) (C)	NAME LOCA	TION TIFI	: 57	10 ON M	1 ETHO N:	D: V scor	e 4.	eijn 7 LIAH					-	
	(х	i) S	EQUE	NCE	DESC	RIPT	ION:	SEQ	ID	NO:	88:						
AAAT	TAAF	AAA A	AAAG	TCAG	r GC	GTTI	TGGG	TAT	CATI	'ATA	GTTT	'AAA'	TT T	CCTT	A A1 Me -1	et	59
ACG Thr	ATT Ilė	TTC Phe	CAT His	GTG Val -10	CTT Leu	ATT Ile	GCC Ala	CAT His	TCA Ser ~5	TCC Ser	AGC Ser	TTC Phe	TCT Ser	TGT Cys 1	GAA Glu		107
		GTT Val 5															155
TAT Tyr	CTT Leu 20	TAT Tyr	TCA Ser	CTT Leu	TTG Leu	GAG Glu 25	TTC Phe	TTT Phe	ATT Ile	CTG Leu	AAT Asn 30	ACA Thr	AGT Ser	CCT Pro	TCG Ser	<b>u</b> .	203
ATG Met 35																	206

- (2) INFORMATION FOR SEQ ID NO: 89:
  - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 186 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:    (A) ORGANISM: Homo Sapiens    (F) TISSUE TYPE: Lymph ganglia</pre>	
(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 85129  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.7  seq WQLLXGFCGSYSA/AQ	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:	
AACTTTCGCT GAGGWGCCGA GGCGACGGGG CTTTGGGTTW YYTCCATTAT ACTCATGTAA	60
TGTTCTTGGT TTGATTTATT CAGT ATG CAC TGG CAG CTT TTG BBA GGC TTC  Met His Trp Gln Leu Leu Xaa Gly Phe  -15  -10	111
TGT GGG AGC TAC TCG GCT GCC CAA GCC GAG GCA CAA ACC CTG CCA GGT Cys Gly Ser Tyr Ser Ala Ala Gln Ala Glu Ala Gln Thr Leu Pro Gly -5 1 5 10	159
CTC CAT AGT AAA TAC AAC ACG CAC GGG Leu His Ser Lys Tyr Asn Thr His Gly 15	186
(2) INFORMATION FOR SEQ ID NO: 90:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 308 base pairs  (3) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Umbilical cord</li></ul>	
(in) promite.	

seq FVFLLFFFSXLXY/FM

(A) NAME/KEY: sig\_peptide(3) LOCATION: 114..224

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

(D) OTHER INFORMATION: score 4.6

(C) IDENTIFICATION METHOD: Von Heijne matrix

									•							
ACAC	CTC	CT F	AAAGO	CCGAC	A TA	AACC	TCTA	CTT	GCA	AGG	GAAT	TTGA	AAA A	AAGAT	rgagaa	60
GCC	ACGTO	GAC F	AAGT(	CATAT	C AC	GATO	CAGI	TTT	TAGA!	AGAT	AWT	TTRA	AGR A		ATG Met	116
						TCA Ser -30										164
						ATA Ile										212
						TAT Tyr										260
						ATG Met										308

# (2) INFORMATION FOR SEQ ID NO: 91:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 438 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 139...321
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.5

seq LVTRLALCQSPRA/GQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

AAGGGAGNNA GGAAGCTGCG CTGCATTCTG CGGGACGAAC CCTGCTCCGC GCGAGAATTT	60
TTTTGATTCC TTCTTATTTG GAGAAATCTC CAGCTGCTCT GATGATAGCC TAAGAAGACT	120
GCATGCTGCT TCCTCTCG ATG CCA AGC CAG ACC CTC TCA CAA CCT CGG ATC  Met Pro Ser Gln Thr Leu Ser Gln Pro Arg Ile  -60 -55	171
TCA GTC CTT CAT GGA GAC CTG GTC CCA GCA GGA ATG GCA GTG CAG GAA Ser Val Leu His Gly Asp Leu Val Pro Ala Gly Met Ala Val Gln Glu -50 -45 -40 -35	219
ATT GGC GCC CAG ATG GTT CTT CCA TGT GAA GTT GTC TCG GGC TCT GGG Ile Gly Ala Gln Met Val Leu Pro Cys Glu Val Val Ser Gly Ser Gly	267

CCC TCT GGG

	-30	-25	-20
	CAC CTG GTA ACC His Leu Val Thr		•
	CAT GGT GCG GAT His Gly Ala Asp 5		Ala Phe Gly Ile
	CAC AGC CAC CGT His Ser His Arg 20		
	AGT GAA TGG ACG Ser Glu Trp Thr 35		438
	FOR SEQ ID NO:	•	
(A) (B) . (C)	INCE CHARACTERIST LENGTH: 278 bas TYPE: NUCLEIC A STRANDEDNESS: DO TOPOLOGY: LINEA	e pairs CID : OUBLE :	·
(ii) MOLE	CULE TYPE: CDNA	•	•
(A)	SINAL SOURCE: ORGANISM: Homo TISSUE TYPE: Ly	~	·
·(B)	CURE:  NAME/KEY: sig_p  LOCATION: 147  IDENTIFICATION  OTHER INFORMATI	260 METHOD: Von Heij	
(xi) SEQ	JENCE DESCRIPTION	: SEQ ID NO: 92:	
AAGACACGGA CAG	ACGGACG CGCAGACCI	T CGGAAGGCAC TG	CGTAGGCA GCCTCCCCGG 60
AGCCCACGAG GCT	CCCCAGC ACCGTTCAC	CT GGTGGGAGGC TG	AGCCGGTG GAAAAGACAC 120
CGGGAAGAGA CTC			PA CAC ACT CTG CCC 173 al His Thr Leu Pro -30
	A GCC GTC GTC AGA y Ala Val Val Arc -25		
	e Thr Val Thr Val		C TCT GGG GTG TGC 269 a Ser Gly Val Cys 1

Pro Ser Gly.

. ....

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 335 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: 276..329
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.5

seq SLLLLGRWLTLTS/SG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:

AATTTTGGHA GTAGAGTCTG TAGTGGTACT AATTAAAATA GTCATGTAGA TAAACTGTTT 60

CTTACTGTTT CAGGACAAGA TGAGTCTATG CCAGATGTAA GTCACCACAC TCATTTACTG 120

ATTTCTTCCT TGAGGATTTT TTGTTGTTAA AAAATTTTTG TGGTTGATCT GCATTCTGTC 180

TTAAACTCTT TATTTCATTG TGGATTATTA ACAGTTGGTC CACGGGCCAC ACTTTAAGCA 240

ACGTCAATCT CTAGTATCCA TCTTAGAGGC AAACC ATG ATC TAT TTA ACC AGT 293

Met 1le Tyr Leu Thr Ser -15

CTC TTA CTA TTG GGT AGA TGG TTA ACC CTC ACA TCA TCT GGG 335

Leu Leu Leu Gly Arg Trp Leu Thr Leu Thr Ser Ser Gly -10

-5

1

- (2) INFORMATION FOR SEQ ID NO: 94:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 363 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord

ı	ix	١	FEATURE:	•

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 292..357
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.4 seq GFLLCPLVCGLRR/WT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:

AACCTCTCTT CCTTTCCTGA GTCGTTGGCG CAGTGACTCG CCACCTCCTC CCTCCTCGTC	60
CCCCCACCGG AGGAGTTTTG CGGTCTGTAG AGAGCTATGC AGGGTGAGGG CCCCTAGACT	120
TCGGCTTTCG CCGCTGTTGG TGGTAGGCTG GAGTTGGGGG TCCCTGGATA CGGTTTTGGC	180
TTTACACCCC CTTTCCAGCA AGCTTCCCGT GGGAATCTGT TCCTTTTCAG GACAGCTGTG	240
ATCCACGTGA GTAAAACTGG GCGTTCCGTC TTGTGCTTTT TCCTCAGGTT C ATG AAC Met Asn	297
TGG AAT GTA AGA GGC ACC AGA GGA TTC CTG CTC TGT CCC CTG GTT TGC Trp Asn Val Arg Gly Thr Arg Gly Phe Leu Leu Cys Pro Leu Val Cys -20 -15 -10 -5	345
GGC TTG CGA CGT TGG ACA Gly Leu Arg Arg Trp Thr	363

#### (2) INFORMATION FOR SEQ ID NO: 95:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 261 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 130..255
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.4

seq LVCLTFITATTHE/QP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

AATTGGGTGC ATACTTTTC TTGGTCAGCA TCTCAGTTTC TATTTCTAAA GTCAAAAGAA 60
GTGCCTCGAT TCCTCCCAAG ACTTGACAAG CCCAGCAGGG TTGGTGGCTT CTTTGCTGTG 120
TTGCTGAAA ATG GAA CAG GCT GCC CTG GAG GTG AGC CCC CTG CCC CGG 171
Met Glu Gln Ala Ala Leu Glu Val Val Ser Pro Leu Pro Arg

PCT/IB98/01237

323

**-40 -35 -30** 

AGA TGT TCA GTG AGA TCA CCT GTG ACT ACA TGC TGT GCT AAG GAC CTT

Arg Cys Ser Val Arg Ser Pro Val Thr Thr Cys Cys Ala Lys Asp Leu

-25

-20

-15

GTG TGC CTC ACC TTC ATC ACT GCA ACA ACC CAT GAG CAG CCG

Val Cys Leu Thr Phe Ile Thr Ala Thr Thr His Glu Gln Pro

-10

-5

1

### (2) INFORMATION FOR SEQ ID NO: 96:

#### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 323 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

#### (vi) ORÍGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Umbilical cord

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 24..275
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.4

seq GLVQLHATXLALG/KV

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

AATACTCTCA TCTGTAAAAT GGG ATG ATA ATC CCA CTA CCC AGC TTA GTG GGC 53

Met Ile Ile Pro Leu Pro Ser Leu Val Gly
-80 -75

TGT TGG GAA GGA GGG AAT GGG AAA GGA CTT ATG GTG TCT GAC ACT ACA

Cys Trp Glu Gly Gly Asn Gly Lys Gly Leu Met Val Ser Asp Thr Thr

-70

-65

-60

TGC TGG ACA CTC GCT TCC TCC AAT GTC CCA TCT CCR TCC CCT GCG CCC 149

Cys Trp Thr Leu Ala Ser Ser Asn Val Pro Ser Pro Ser Pro Ala Pro

-55 -50 -45

ACC CTG GGG AGA GGN GCC CCC TCC CAT ACT CCC CAG AAG AAG CCC ACC

Thr Leu Gly Arg Gly Ala Pro Ser His Thr Pro Gln Lys Lys Pro Thr

-40

-35

-30

ATA CCT GGT GCC CGC CAC CGC CCC ATC ATT CTT CCC AAG GGG CTC GTC

1le Pro Gly Ala Arg His Arg Pro Ile Ile Leu Pro Lys Gly Leu Val
-25
-20
-15

CAG CTC CAC GCC ACA YCA CTC GCC CTT GGC AAA GTC TGT CTC CCC CAC

Gln Leu His Ala Thr Xaa Leu Ala Leu Gly Lys Val Cys Leu Pro His

-10

-5

1

5

GTA CCG CAC CAC GCY AGT CTT CGT CCC GCA

235

\* \*\*\*

Val Pro His His Ala Ser Leu Arg Pro Ala 10 15

121	INFORMATION	FOR	SEO	TD	NO.	97 .
121	THEORMATION	202	JUL	ΤU	NO.	<i>71</i> ;

(i	SEQUENCE	CHARACTERISTICS:
----	----------	------------------

- (A) LENGTH: 235 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymphocytes

#### (ix) FEATURE:

- (A) NAME/KEY: sig peptide
- (B) LOCATION: 65..190
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.3

seq IQTVHIALPGSLG/HP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

#### ATATGGTAAT TAMVAATATG TTTATGTACC CTGAATCATG TAAATATTTG AGCTTTCTCT 60

- AAAA ATG AGT ATG AGA CTA TCT GGA GAA AGA ATT TAT CTC CTG TTA GAG 109

  Met Ser Met Arg Leu Ser Gly Glu Arg Ile Tyr Leu Leu Leu Glu
  -40 -35 -30
- GTT TGG CTG CCT TRW CTC AAT TTT GAG TCA GTT CTT CAT TTT ATC CAA

  Val Trp Leu Pro Xaa Leu Asn Phe Glu Ser Val Leu His Phe Ile Gln

  -25

  -20

  -15
- ACT GTC CAC ATT GCC CTC CCT GGA AGT CTG GGC CAC CCA ATG GGC CCC

  Thr Val His Ile Ala Leu Pro Gly Ser Leu Gly His Pro Met Gly Pro

  -10 -5 1 5

TGT GCC TGC CGC CCC TCT TTA GCC CAC CCG
Cys Ala Cys Arg Pro Ser Leu Ala His Pro
10 15

(2) INFORMATION FOR SEQ ID NO: 98:

### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 197 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens

WO 99/065	53 PCT/II	B98/01
	(F) TISSUE TYPE: Lymph ganglia	
(ix)	FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 144191  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.3  seq LLLFCFMPVVINP/DR	
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 98:	
ATCATTTGGC	AGAGAAGAGA GAAGGGTATG AGTTGCCAGG TAGTGGATGC AGATGGAAGC	60
GCTGGTGGGC	CCATTGGTTG ATCATTGGTT GGGACCATCT TACACAGAAA GTTCATCCTA	120
TTGCCCTTTC	CCACTGTGTT AAT ATG GGA ACA CTC CTT CTC TTC TGT TTT ATG  Met Gly Thr Leu Leu Leu Phe Cys Phe Met  -15 -10	173
	Ile Asn Pro Asp Arg	197
(2) INFORMA	TION FOR SEQ ID NO: 99:	
(ii)	EQUENCE CHARACTERISTICS:  (A) LENGTH: 253 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR  MOLECULE TYPE: CDNA  ORIGINAL SOURCE:  (A) ORGANISM: Homo Sapiens  (F) TISSUE TYPE: Lymph ganglia	
•	FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 86151  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.1  seq GIYLQLFFLSIVS/QP	
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 99:	
AGCAGTGCVG	AAGAGAAAAG CAGAGATAAG CAAGGCTCCG CAGCAGCCTC CTTTCTAACT	60
mex coomece	CACACCORGO COAGO ATG GTT GTC CTG AAT CCA ATG ACT TTG	112

Met Val Val Leu Asn Pro Met Thr Leu

-15

160

208

-20

GGA ATT TAT CTT CAG CTT TTC TTC CTC TCT ATC GTG TCT CAG CCG ACT

Gly Ile Tyr Leu Gln Leu Phe Phe Leu Ser Ile Val Ser Gln Pro Thr

TTC ATC AAC AGC GTT CTT CCA ATC TCA GCA GCC CTT CCC AGC CTG GAT

-10

. ....

Phe	Ile 5	Asn	Ser	Val	Leu	Pro 10	Ile	Ser	Ala	Ala	Leu 15	Pro	Ser	Leu	Asp	
				GGT Gly												253

# (2) INFORMATION FOR SEQ ID NO: 100:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 358 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

# (ii) MOLECULE TYPE: CDNA

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia-

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 212..319
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.1

seq HWLFLASLSGIKT/YQ

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:

ATCCCCAWNS CACTCTCTCA CAGAGACTGT TCTTTTCCTT CTGAGACCCT ACTCCAGCTT	60
GTAGTTCTAA ATCTGTGATT ATGCACTGTC TGTCTTCCTC TTGAGGTCAG GGGCCATTTC	120
TTTTGTTCTC TGCTATGCTC AGGACCCAGA TCAAAGGAGC TCAGTAACTA TTTACAGGCG	180
TACATCATAT GTGGAGGACA CTTATGCTGT G ATG GCC CCA CAC ACA GCT TCC  Met Ala Pro His Thr Ala Ser  -35 -30	232
TTT GGG GTC TGT CCC CTG CTC TCC GTT ACC CGC GTG GTA GCC ACT GAG  Phe Gly Val Cys Pro Leu Leu Ser Val Thr Arg Val Val Ala Thr Glu  -25 -20 -15	280
CAC TGG CTC TTC CTG GCT TCA CTC TCT GGC ATC AAA ACT TAT CAG TCC His Trp Leu Phe Leu Ala Ser Leu Ser Gly Ile Lys Thr Tyr Gln Ser -10 -5 1	328
TAC ATC TCA GTC TTT TGC AAG GTG ACT GGG Tyr Ile Ser Val Phe Cys Lys Val Thr Gly 5 10	358

## (2) INFORMATION FOR SEQ ID NO: 101:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 181 base pairs

MAN THE THE		
WO 99/06553	75 PCT	/IB98/012
(C)	TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLE	CULE TYPE: CDNA	
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Lymph ganglia	
(B) (C)	URE:  NAME/KEY: sig_peptide  LOCATION: 113172  IDENTIFICATION METHOD: Von Heijne matrix  OTHER INFORMATION: score 4.1  seq SLPCLSFCTLCLV/TP	
(xi) SEQU	ENCE DESCRIPTION: SEQ ID NO: 101:	
ATCCCATCTT AGCT	GCCATC CCATCCTGTA TGTAGATACC CTGTTCATCT CTCTCAAGAT	60
CTTTATTCTA GACC	TTCTTT GTCTTTCTTG GGCTCCAACA CCTCACACCA AG ATG TCT Met Ser -20	
	CCC TCC TTA CCC TGC TTG AGT TTC TGT ACC CTG TGC Pro Ser Leu Pro Cys Leu Ser Phe Cys Thr Leu Cys -10 -5	166
TTG GTC ACC CCC Leu Val Thr Pro		181
(2) INFORMATION	FOR SEQ ID NO: 102:	
(i) SEQUE	CNCE CHARACTERISTICS: LENGTH: 191 base pairs	

- (2) INFORM
  - (i)

    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: 117..182
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1
      - seq LAGFLLVLYVCLP/HA
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:

CACC	CCTTTTG TAATTAATCT CTGGTGTCCA CCGCCCACTG TTACCCAAGT GAATGC ATG Met	119
Pro	CTC CCC ACC TGG GCT CCG ACC CTG GCA GGG TTC CTG CTT GTC TTG Leu Pro Thr Trp Ala Pro Thr Leu Ala Gly Phe Leu Leu Val Leu -20 -15 -10	167
	GTC TGT CTC CCT CAC GCC GGG Val Cys Leu Pro His Ala Gly 1	191
(2)	INFORMATION FOR SEQ ID NO: 103:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 129 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
	(ii) MOLECULE TYPE: CDNA	
	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Homo Sapiens  (F) TISSUE TYPE: Umbilical cord	
	<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 3181     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4.1</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:	
ACAC	CTATGAT TTTATAAAAC AATTTTTCT ATG AAC CTT TAC TTA CTT GAC TGG  Met Asn Leu Tyr Leu Leu Asp Trp  -15 -10	54
Ile	GGA CTA AAA GCA CTG ATC AGA GGC CAC GAC ATA AAA ATT CAG TCC Gly Leu Lys Ala Leu Ile Arg Gly His Asp Ile Lys Ile Gln Ser -5 1 5	102
CTT	TGT CCT TCC CCG TGC CTC CCA AGG Cys Pro Ser Pro Cys Leu Pro Arq 10 15	129
(2)	INFORMATION FOR SEQ ID NO: 104:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 198 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	

(ii) MOLECULE TYPE: CDNA

106

<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Lymph ganglia</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 28189     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4.1</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:	
ATCATTTGGC AGAGAAGAGA GRWGGGT ATG AGT TGC CAK GTA SWK GAT GCA RSS Met Ser Cys Xaa Val Xaa Asp Ala Xaa -50	54
ARG CGC TGG TGG GCC CAT TSG TTG ATC ATT GGW TGG GRC CAT CTT ACA  Xaa Arg Trp Trp Ala His Xaa Leu Ile Ile Gly Trp Xaa His Leu Thr  -45 -35 -30	102
CAG AAA GTT CAT CCT ATT GCC CTT TCC CAC TGT GTT AAT ATG GGA ACA Gln Lys Val His Pro Ile Ala Leu Ser His Cys Val Asn Met Gly Thr -25 -20 -15	150
CTC CTT CTC TGT TTT ATG CCT GTA GTG ATT AAC CCG GAC ARM GGG Leu Leu Phe Cys Phe Met Pro Val Val Ile Asn Pro Asp Xaa Gly -10 -5 1	198
(2) INFORMATION FOR SEQ ID NO: 105:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 148 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Lymph ganglia</pre>	•
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 59124     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:	
AGATTACAAA AAAAAAATTC TCAAGTGAAT AAAGTCCATT GATAGATATT TTGTTTAA	58

ATG GTA CCA AAT CTG TGT GGA AGG CAA ATT TTG GCT TTC CAG ACA TTC

Met Val Pro Asn Leu Cys Gly Arg Gln Ile Leu Ala Phe Gln Thr Phe

-20	0	-15	-10
		CTT TTT CAA CTG G Leu Phe Gln Leu A 5	

#### (2) INFORMATION FOR SEQ ID NO: 106:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 240 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 82..123
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4

seq FSLIIFFFPPSSP/XA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

ACAACCTKHN TCTCMCCTGT	ATCTTTGTCA TGTCAGTCA	C TGATATCAGC ATCTGCCCAG 60
TTGCTCAGGC CAAAACCTTA		e Ile Phe Phe Pro
CCC TCA TCC CCW AMR GC Pro Ser Ser Pro Xaa Al		
TTA TAC CTG AAA TTT GT Leu Tyr Leu Lys Phe Va 15		
TCA GAG TGT GTT CAT AS Ser Glu Cys Val His I: 30	•	

## (2) INFORMATION FOR SEQ ID NO: 107:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 331 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA

<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Lymphocytes</li></ul>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 242310     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:	•
ACATCCAATA ATCATTTATA AAGATCTCTA ACAGGCCAGT CAGTATACAG AGTACCAGAT	60
TAAAAATAAA TGTAGCACCA GTTTTTCAGA AATTATTATG TGTCTATAAT TAGGGTAATT	120
ACATTTAGAA GATCTTTTTG ATGATCTCCT TAAAGTCAGC AACTGTCTTT TTCATCTTTTG	180
TTTACCTAGT ACCTGGAATG GAGATAGGCG TTTAGCACTT AAATGTTTAC TGMATATTCT	240
T ATG AGT GCC TTT TAT CTT TCC TAC TCC TTG TTG CAT TGC TTA CTT ATT  Met Ser Ala Phe Tyr Leu Ser Tyr Ser Leu Leu His Cys Leu Leu Ile  -20 -15 -10	289 ;
GTT TTT ATT TTA GTT GAG TTT TGT AAG AAA TTG ACT TAC TTT Val Phe Ile Leu Val Glu Phe Cys Lys Leu Thr Tyr Phe  -5 1 5	331 <sup>:</sup>
(2) INFORMATION FOR SEQ ID NO: 108:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 315 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Lymph ganglia</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 160249     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:	

AGCAAACTCT TAAGGTCACT TTCTGAAGGC GGCCTCATCA CAGTCGGAGG TATCATGATA 60
TTAGCTGGTT TGACATCAAG TCATTTGTGA GTCATCAGAT CTTCTCCTGA AAATGGGAGA 120

P/	T	ΛB	90	'n	123	7
	- 14	,,,,,	70	w		•

Met Ala Glu Ala Lys -30	174
CTT GTC CAA GGT TCA CTT GTA GCC CCT CAG CGT CAS TCA GCT GGT GTC Leu Val Gln Gly Ser Leu Val Ala Pro Gln Arg Xaa Ser Ala Gly Val -25 -10	222
GTC CTG ACC ATG GAC GGC GCG TCG GCC GAG CAA GAT GGC CTC CAG GAG Val Leu Thr Met Asp Gly Ala Ser Ala Glu Gln Asp Gly Leu Gln Glu -5 1 5	270
GAC AGA TCC CAC AGT GGC CCC TCG TCT CTC CCC GAG GCC CAC CGG Asp Arg Ser His Ser Gly Pro Ser Ser Leu Pro Glu Ala His Arg 10 15 20	315
(2) INFORMATION FOR SEQ ID NO: 109:	
(i) SEQUENCE CHARACTERISTICS:	
(A) LENGTH: 222 base pairs (B) TYPE: NUCLEIC ACID	
(C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
(vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens	
(F) TISSUE TYPE: Umbilical cord	
·	
(ix) FEATURE: (A) NAME/KEY: sig peptide	
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177	
(A) NAME/KEY: sig_peptide	
<ul><li>(A) NAME/KEY: sig_peptide</li><li>(B) LOCATION: 1177</li><li>(C) IDENTIFICATION METHOD: Von Heijne matrix</li><li>(D) OTHER INFORMATION: score 4</li></ul>	
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq VLLTISTNASVLG/DG  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:	48
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq VLLTISTNASVLG/DG	48
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq VLLTISTNASVLG/DG  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:  ATG AAA GGA GTA GGG CCT GAG CAG CTG AAT GAT GGA GCG CCA TCA AAT Met Lys Gly Val Gly Pro Glu Gln Leu Asn Asp Gly Ala Pro Ser Asn -55 -50 -45  GAG ATT GAA ATG ACT CCA TGT TTT TTC AGT GAG TTC CTT CTA TTG GAC	48
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq VLLTISTNASVLG/DG  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:  ATG AAA GGA GTA GGG CCT GAG CAG CTG AAT GAT GGA GCG CCA TCA AAT Met Lys Gly Val Gly Pro Glu Gln Leu Asn Asp Gly Ala Pro Ser Asn -55 -50 -45	
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq VLLTISTNASVLG/DG  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:  ATG AAA GGA GTA GGG CCT GAG CAG CTG AAT GAT GGA GCG CCA TCA AAT Met Lys Gly Val Gly Pro Glu Gln Leu Asn Asp Gly Ala Pro Ser Asn -55 -50 -45  GAG ATT GAA ATG ACT CCA TGT TTT TTC AGT GAG TTC CTT CTA TTG GAC Glu Ile Glu Met Thr Pro Cys Phe Phe Ser Glu Phe Leu Leu Leu Asp -40 -35 -30  GTT GGT GTT GTT AAT ATA GTA GTT ATT AAA ATG TCT TAT AAT GTC CTG	
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq VLLTISTNASVLG/DG  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:  ATG AAA GGA GTA GGG CCT GAG CAG CTG AAT GAT GGA GCG CCA TCA AAT Met Lys Gly Val Gly Pro Glu Gln Leu Asn Asp Gly Ala Pro Ser Asn -55 -50 -45  GAG ATT GAA ATG ACT CCA TGT TTT TTC AGT GAG TTC CTT CTA TTG GAC Glu Ile Glu Met Thr Pro Cys Phe Phe Ser Glu Phe Leu Leu Asp -40 -35 -30	96
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq VLLTISTNASVLG/DG  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:  ATG AAA GGA GTA GGG CCT GAG CAG CTG AAT GAT GGA GCG CCA TCA AAT Met Lys Gly Val Gly Pro Glu Gln Leu Asn Asp Gly Ala Pro Ser Asn -55 -50 -45  GAG ATT GAA ATG ACT CCA TGT TTT TTC AGT GAG TTC CTT CTA TTG GAC Glu Ile Glu Met Thr Pro Cys Phe Phe Ser Glu Phe Leu Leu Asp -40 -35 -30  GTT GGT GTT GTT AAT ATA GTA GTT ATT AAA ATG TCT TAT AAT GTC CTG Val Gly Val Val Asn Ile Val Val Ile Lys Met Ser Tyr Asn Val Leu -25 -20 -15  TTA ACG ATT AGT ACT AAT GCC TCT GTA CTT GGT GAT GGT GCT CAT AGA	96
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq VLLTISTNASVLG/DG  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:  ATG AAA GGA GTA GGG CCT GAG CAG CTG AAT GAT GGA GCG CCA TCA AAT Met Lys Gly Val Gly Pro Glu Gln Leu Asn Asp Gly Ala Pro Ser Asn -55 -50 -45  GAG ATT GAA ATG ACT CCA TGT TTT TTC AGT GAG TTC CTT CTA TTG GAC Glu Ile Glu Met Thr Pro Cys Phe Phe Ser Glu Phe Leu Leu Leu Asp -40 -35 -30  GTT GGT GTT GTT AAT ATA GTA GTT ATT AAA ATG TCT TAT AAT GTC CTG Val Gly Val Val Asn Ile Val Val Ile Lys Met Ser Tyr Asn Val Leu -25 -20 -15	96 144
(A) NAME/KEY: sig_peptide (B) LOCATION: 1177 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq VLLTISTNASVLG/DG  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:  ATG AAA GGA GTA GGG CCT GAG CAG CTG AAT GAT GGA GCG CCA TCA AAT Met Lys Gly Val Gly Pro Glu Gln Leu Asn Asp Gly Ala Pro Ser Asn -55 -50 -45  GAG ATT GAA ATG ACT CCA TGT TTT TTC AGT GAG TTC CTT CTA TTG GAC Glu Ile Glu Met Thr Pro Cys Phe Phe Ser Glu Phe Leu Leu Leu Asp -40 -35 -30  GTT GGT GTT GTT AAT ATA GTA GTT ATT AAA ATG TCT TAT AAT GTC CTG Val Gly Val Val Asn Ile Val Val Ile Lys Met Ser Tyr Asn Val Leu -25 -20 -15  TTA ACG ATT AGT ACT AAT GCC TCT GTA CTT GGT GAT GGT GCT CAT AGA Leu Thr Ile Ser Thr Asn Ala Ser Val Leu Gly Asp Gly Ala His Arg	96 144

(2)	INFORMATION	FOR	SEQ	ID	NO:	110:
-----	-------------	-----	-----	----	-----	------

,	÷	١	SECHENCE	CHARACTERISTICS	
•	1	1	ファクロアいてか	CUMUMCIENTALICA	=

- (A) LENGTH: 464 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

## (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Umbilical cord

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 255..389
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.8

seq QLFWVTASTFCRS/DI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

AAGAT TAAGG	AAAGCIGCCC	MUMCANIUC CA	AIGCCCICA	IIIIIICAGII I	CAGICATIA 60
TTTTTCTCAG	CAGTGTCCTT 1	TGGCTTCAC TO	STGTCTTCT	AACATCATCA G	CCAAATTGT 120
TTCTTTCTTT	TGTAATCTGT A	AGTTTCAAAA TA	AATAGGAGT '	TGTTTTGCTT T	CAGAAAAAG 180
ACAATTATAA	TGTTGATTTG (	STTCTTTTAA AF	AAACTAAAC	ACACCCTCTG G	AGATTCTAA 240
TTTACTCCGT	ATTC ATG CTC Met Les	AGG AAA CTA Arg Lys Leu			
	C TCA AAC CCC u Ser Asn Pro -30		n Glu Val		
	C CAT CAG CT r His Gln Le 5				
	A GCT ACT AT e Ala Thr Me	-			
	C TCA ACA TT se Ser Thr Ph 20				464

## (2) INFORMATION FOR SEQ ID NO: 111:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 268 base pairs

82	• • • • • • • • • • • • • • • • • • • •
(B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Lymph ganglia</li></ul>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 215259     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 3.8</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:	
ATGATGGGGT GTTAGTAAAA GTGATACTAG TTCTTGATGA TGGTTATCTC TTTGCCTT	
ATTCAGGAGT TAAAAATTAA TGAGGGCCTT TTCTGAACTG TAAAGATATG GTATTTAG	SCA 120
GTTCTTAATA TACTGAGGGT TTCTCATTCT CTCTTTTTGA TTATGTTGTA TTTGGCAC	AT 180
GGTTATTTGG GGACTACTTA CATTCTTAAA TTGA ATG TAT CCT TTG ATT CTC C  Met Tyr Pro Leu Ile Leu I -15 -10	
CCT CTT AAC CCA TTT GTG CTG CAG GTT GCT GGG Pro Leu Asn Pro Phe Val Leu Gln Val Ala Gly -5	268
(2) INFORMATION FOR SEQ ID NO: 112:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 440 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	

- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 240..308
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.8

seq RGFVAVGLGQISA/SP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:

TCTGTTGCTC TGGGTTGCAG CCTCTASGGG TGAGATCGTG CTGACTCAGT CTCCGGACTT	.120
TCAGCCTGTG ACTCCTGGCG ASMGCGTCAC TATCACCTGC CGGGCCAGTC AAGACATAAG	180
TYACAAATTA CATTGGTACC AGCAGAAGCC TGGTCAGTCT CCAAGGCTCC TCGTCAAAT	239
ATG CTT CTC AGA CCC TCT CCG GGG TCC CCT CGA GGT TTC GTG GCA GTG Met Leu Arg Pro Ser Pro Gly Ser Pro Arg Gly Phe Val Ala Val -20 -15 -10	287
GGA CTG GGA CAG ATT TCA GCC TCG CCA TCG ATG GCC TGC AAA CTG ACG Gly Leu Gly Gln Ile Ser Ala Ser Pro Ser Met Ala Cys Lys Leu Thr -5	335
ATT TTG CAA CAT ACT TCT GTC TTC AGA GTA GTC TTC CGT ACA CCT Ile Leu Gln His Thr Ser Val Phe Arg Val Val Val Phe Arg Thr Pro 10 15 20 25	383
TTG GTC AGG GGA CCA CTC TCC AGG TCA AAC GAG CTG TGG CTG CAC CAT Leu Val Arg Gly Pro Leu Ser Arg Ser Asn Glu Leu Trp Leu His His 30 35 40	431
CTG TCT TCA Leu Ser Ser	440
i	:
(2) INFORMATION FOR SEQ ID NO: 113:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 167 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	٠
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Umbilical cord</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 93146     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 3.8</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:	
AATACTAATT CCTACCAGTC CTCACGAGGA GGGTGACACA CACCCTGTTC CCACTTGAGA	60
GAGGGCATCT GCAGGGGTGG AGGGGAGACC CC ATG GCT CGG CCT GGT GCC ACA  Met Ala Arg Pro Gly Ala Thr  -15	113
GCC TGC GGG CCT GCC GCC CAC CAG TGC TCT GCG GTC CCA CTG TGG TCC Ala Cys Gly Pro Ala Ala His Gln Cys Ser Ala Val Pro Leu Trp Ser -10 -5 1 5	161

CCT GGG Pro Gly

-

167

	INFORMATION	EOD	CEO	TO	NO.	714.
{ Z ].	INFORMATION	ruk	250	TD	NO:	114:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 259 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 191..247
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.8

seq LSLCIXXLEHLFT/WP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

ACACTGAATC TTCTAGAGCC ACGGTAGCCA ACCTTTTAAA ATCAGTTGAG GGCACTTAAA 60

AAAATACATC AGTATTTTTA CACCTGATTT TTACACCTGG GCCCCAGCCT TGTGCAACAG 120

AACCTAGGGG TGGAGTCTAA GCATGGACAG TTTTTAAAGC CCCAGGCAGC CAGGGCTGAG 180

GACCTTGGCG ATG GAG CCT GTW AGT TCG CTT TCC TTG TGT ATA TKG WCT

Met Glu Pro Val Ser Ser Leu Ser Leu Cys Ile Xaa Xaa

-15
-10

CTT GAG CAT CTC TTC ACA TGG CCC AAA GGG Leu Glù His Leu Phe Thr Trp Pro Lys Gly -5 259

### (2) INFORMATION FOR SEQ ID NO: 115:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 203 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE: .
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:

WO 99/06553	85 PCT	[/IB98/01
(B) (C)	NAME/KEY: sig_peptide LOCATION: 120176 IDENTIFICATION METHOD: Von Heijne matrix OTHER INFORMATION: score 3.8 seq WCSAAAWRSPLSA/AT	
(xi) SEQUE	ENCE DESCRIPTION: SEQ ID NO: 115:	
ACTCGCCGGC GCCA	GGCAGT GGGAAGTCAG GTTCTTCCGC CACCTCCCAG CCAGGACTCT	60
GCCACCCTCC CTCAC	GGATGC CTGAGGGCCC CGAGCTGCAC CTGGCCAGCC AGTKTGTGA	119
	GGG CGC TGG TGT TCG GCG GCT GCG TGG AGA AGT CCT Gly Arg Trp Cys Ser Ala Ala Ala Trp Arg Ser Pro -15 -10 -5	167
	ACC CTG AAG TGC CCT TTG AGA GGG Thr Leu Lys Cys Pro Leu Arg Gly 5	203
(2) INFORMATION	FOR SEQ ID NO: 116:	
(A) (B) (C)	NCE CHARACTERISTICS: LENGTH: 66 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLE	CULE TYPE: CDNA	
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Lymph ganglia	
(B) (C) - (D)	NAME/KEY: sig_peptide LOCATION: 1057 IDENTIFICATION METHOD: Von Heijne matrix OTHER INFORMATION: score 3.7 seq CAYVLFFFNGCLY/RR	• .
(xi) SEQU	ENCE DESCRIPTION: SEQ ID NO: 116:	
	GG TTG TGT GCG TAT GTA TTA TTT TTT TAAT GGA TGT	

-15 -10

TTA TAT AGG AGA AAG Leu Tyr Arg Arg Lys 66

- (2) INFORMATION FOR SEQ ID NO: 117:
  - (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 289 base pairs

The state of the s	and the second of the second o	
WO 99/06553	86 PCT/IB98/0	)1
(B)	TYPE: NUCLEIC ACID	
	STRANDEDNESS: DOUBLE	
	TOPOLOGY: LINEAR	
(ii) MOLE	CULE TYPE: CDNA	
(vi) ORIG	INAL SOURCE:	
(A)	ORGANISM: Homo Sapiens	
(F)	TISSUE TYPE: Lymph ganglia	
(ix) FEAT	URE:	
(A)	NAME/KEY: sig_peptide	
	LOCATION: 152196	
(C)	IDENTIFICATION METHOD: Von Heijne matrix	
(D)	OTHER INFORMATION: score 3.6	
	seq LLHRAVVLRLQQA/CR	
(xi) SEQU	ENCE DESCRIPTION: SEQ ID NO: 117:	
1		
AAAAATTGC AGTG	CTGAAG ACACTGGACC CGCAAAAGGC TGTCCCTCCC AAACCTGGGA 60	
TTCTGGGCTC ACTG	AGTTCA CCTGCGAGTC AGCCCTACCT GCACTGCTCT GGTCTAGTAC 120	
AAACAGGCTG CTGG	CATTGA GGTCTGCTAC A ATG CTG CTG CTG CAC AGA GCT 172	
i	Met Leu Leu His Arg Ala	
	-15 -10	
GTG GTC CTC AGG	CTC CAA CAG GCC TGC AGA CCG ACC TCT CTT CCA GAC 220	
Val Val Leu Arg	Leu Gln Gln Ala Cys Arg Pro Thr Ser Leu Pro Asp	
-5	1 5	
TCA AGT CAA TCC	CCT CAA GGA TCT GCA TTC AGG CCT GCT CCA CAA ATG 268	
	Pro Gln Gly Ser Ala Phe Arg Pro Ala Pro Gln Met	
10	15 20	
ATT CAT TTC AGO	CCC CTT GVS 289	
Ile His Phe Ser		
25	30	
(2) INFORMATION	FOR SEQ ID NO: 118:	
(i) SEQUE	NCE CHARACTERISTICS:	

## (2) INFORMA

- (i) S
  - (A) LENGTH: 268 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 110..205
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.6

---

#### seq SLVPSMCFHVTNS/IK

(xi)	SEQUENCE	DESCRIPTION:	SEQ	ID	NO:	118:
------	----------	--------------	-----	----	-----	------

ACGCCAAATG ATTATACTCG GGACACCTGA CCCAGTTTCT TCAACAAATA TATGGAGGGA AACGTGTGTV TAGGACGGGG GTRTTTTAAA TAAAAAGGGC TTTAAGACG ATG GAA ATG 118 Met Glu Met TTT GGT TWR RTT GAA AAA GAT TTT TCA TCA GTG GAA GGG GTT CTA TRG 166 Phe Gly Xaa Xaa Glu Lys Asp Phe Ser Ser Val Glu Gly Val Leu Xaa ~20 AGC CTG GTA CCT TCA ATG TGT TTC CAT GTT ACC AAC TCC ATA AAG ATG 214 Ser Leu Val Pro Ser Met Cys Phe His Val Thr Asn Ser Ile Lys Met CCC TGG TTT CCC AGC CAA CCA GGT ACT TGC ACC CAG AAG GAT TGC CCT 262 Pro Trp Phe Pro Ser Gln Pro Gly Thr Cys Thr Gln Lys Asp Cys Pro 10 CCG AAG 268 Pro Lys 20 (2) INFORMATION FOR SEQ ID NO: 119:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 148 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: 5..142
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.6

seq LLGVHASFQMSVA/AR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

AATT ATG CAG ATG CAC GGC TGG AGG TGG GAT CCA CAC AGC TCA GAA CAG

Met Gln Met His Gly Trp Arg Trp Asp Pro His Ser Ser Glu Gln

-45

-40

-35

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymphocytes
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 89..190
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.6

seq VGTGVLTSRLARA/TP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

TCGAACTTGG AGATAGCTGG TTCTCCTCGA AATAGCTTTA GGGCTAGCGT GTAGTGTTAA 60

GTAGTGGTGG TAGAGCACTG AATATGGA ATG GCC TCG CCT AGG GGT ACT GAC

Met Ala Ser Pro Arg Gly Thr Asp

-30

TAT AAT CAA ACT CCG AAT ACC ACT ATG TAT TGC TAT GCA GTC GGA ACC

Tyr Asn Gln Thr Pro Asn Thr Thr Met Tyr Cys Tyr Ala Val Gly Thr

-23

GGG GTG CTA ACG TCC CGG CTC GCG AGG GCA ACA CCC GGG

Gly Val Leu Thr Ser Arg Leu Ala Arg Ala Thr Pro Gly

-10

-5

1

112

#### (2) INFORMATION FOR SEQ ID NO: 121:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 356 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE:	Lymphocytes
------------------	-------------

(j	(x)	FEATURE:	•
----	-----	----------	---

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 144..269

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 3.6

seq LHCLCPFPALFLS/VT

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

AAAACTGCT	ATGCTTCC	TACTACTCC	GMTATACTGG	CCTCTTGCTT TCS	CYTCAGC 60
TTACTAATA	TATTCCTC	CC TTAGAGCCTT	TGCACTGGTT	TTTCCCTCTG CTT	AAAGCAT 120
CCCCTCCC	ACCCCACAT	•		C AGC TCC TTC u Ser Ser Phe -35	
	s Tyr His			AGC ATT CTA TT Ser Ile Leu Le -20	
				GCT TTA TTT CT Ala Leu Phe Le -5	
				AAC TTA TAT AT Asn Leu Tyr Il 1	
	l Cys Leu	CTC TAC TGG Leu Tyr Trp	Asn Val Leu		356

## (2) INFORMATION FOR SEQ ID NO: 122:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 155 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 63..128
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.5

seq ILVPWWLPPFVYT/AI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

AGAAAAAAA CTTCAAAATT GAGGATCTCT GTAATTTAAA TCCTACTTAA CAAAGTAAAT	60
GC ATG AAC AGG TTG TCT AAA CAT CTT ATT ATA CTT GTT CCT TGG TGG Met Asn Arg Leu Ser Lys His Leu Ile Ile Leu Val Pro Trp Trp -20 -15 -10	107
CTT CCT CCC TTT GTT TAC ACT GCC ATA TCC TAT GTC CAA CTC CCA GGG Leu Pro Pro Phe Val Tyr Thr Ala Ile Ser Tyr Val Gln Leu Pro Gly -5 1 5	155
(2) INFORMATION FOR SEQ ID NO: 123:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 217 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Lymph ganglia</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 122208     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 3.5</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:	
ACCTCTGCAC TCCTGCCCGC CCTGCCCCCG GCCTGTCTGC TGGAGGTGTG AACCCACATC	60
CCTGCCCCCA GGGCCACCTG CAGGACGCCG ACACCTACCC CTCAGCAGAC GCCGGAGAGA	120
A ATG AGT AGC AAC AAA GAG CAG CGG TCA GCA GTG TTC GTG ATC CTC TTT Met Ser Ser Asn Lys Glu Gln Arg Ser Ala Val Phe Val Ile Leu Phe -25 -20 -15	169
GCC CTC ATC ACC ATC CTC ATC CTC TAC AGC TCC AAC AGT GCC ATT GGG Ala Leu Ile Thr Ile Leu Ile Leu Tyr Ser Ser Asn Ser Ala Ile Gly -10 -5 1	217
(2) INFORMATION FOR SEQ ID NO: 124:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 367 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	

(ii) MOLECULE TYPE: CDNA

w-E --

(vi).ORIGINAL	SOURCE:
---------------	---------

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymphocytes

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 149..352
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.5

seq CLFLSPQSFLVLS/WA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

ATAACATTTG GTGCCGAAAG CCCGGGATAG GGGAACTCCT CCGGCAGACC TCTCCTCTAT	60
CCTCCCGGTA CCCACGTTCT CCCATGCAAG AGACTTCCCT CGCCCTCAGG ACCTCAGACC	120
AGCTCCGCGA GCACTCCGGC CTCTGTCT ATG GAT ATG AAA TCC AAC ACC GGT Met Asp Met Lys Ser Asn Thr Gly -65	172
CAC GGA CTC TTC TTG GGG AGA CAG CCT TCC TTC AGT GTT CGG TCA ATG His Gly Leu Phe Leu Gly Arg Gln Pro Ser Phe Ser Val Arg Ser Met -60 -55 -45	220
CCC GGG ACG CCC GCC TTG GCC ATT TGC CAG CCA CAC AAC CCA GGA CCT Pro Gly Thr Pro Ala Leu Ala Ile Cys Gln Pro His Asn Pro Gly Pro -40 -35 -30	268
CCA ATG GGG ACG CCC ACT GAG GAT CCT AGT GGT TGC TCT TTT CCT TGT Pro Met Gly Thr Pro Thr Glu Asp Pro Ser Gly Cys Ser Phe Pro Cys -25 -20 -15	316
CTC TTT CTT TCC CCC CAG TCT TTC CTT GTT CTA TCA TGG GCA ATT TCC Leu Phe Leu Ser Pro Gln Ser Phe Leu Val Leu Ser Trp Ala Ile Ser -10	364
CGC Arg 5	367

# (2) INFORMATION FOR SEQ ID NO: 125:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 300 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 193..279

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.5 seq LSLSSTLLLTSHH/HQ
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

ACAACGCACA CATCGTGAGA CGTTTTTCAA GACACCCGGC AGCCTTGGAG ACCCTGTCCT ഹ GAAGAGAAGA GAAAGGAACC AGTCACGAAA CACCAGCTCG GCCCAGAGGA GACTAGAAAT 120 CCCCAGCGGC GGCGCTGACT AACCTGCCGC TTTGCCAGGT GGGGGTGGGA TCAAACGCCC 180 TGAGAGTCCC GG ATG TCC GAG GCG GGA TGC AAA CCA TCC CGT CCT GAG CAC 231 Met Ser Glu Ala Gly Cys Lys Pro Ser Arg Pro Glu His -25 GGG TCC TTC CTC TCT TCA TCC ACA CTT CTG TTA ACT TCC CAC CAC 279 Gly Ser Phe Leu Ser Leu Ser Ser Thr Leu Leu Leu Thr Ser His His -15 - -10 CAT CAA TCA TCT GAT TTC GGG 300 His Gln Ser Ser Asp Phe Gly

### (2) INFORMATION FOR SEQ ID NO: 126:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 422 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 255..284
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 201..230

. id R72787

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
    - (B) LOCATION: 121..152
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 90 region 1..32

id H73816

est

- (ix) FEATURE:
  - (A) NAME/KEY: other

(B)	LOCATION: 241283	
(C)	IDENTIFICATION METH	HOD: blastn
(D)	OTHER INFORMATION:	identity 93
		region 161203
	•	id SSC1D10
		Act

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 81..137
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 12.8

seq XVFLVALLRGVQC/QV

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

>>====================================	<b>C</b> O
AAGCHCTGGG AGAGGAGCCC AGCACTAGAA GTCGGCGGWG TTTCCATTCG GTGATCAGCA	60
CTGAACACAG AGGACTCACC ATG GAG TCC GGG MWG GGG TGR GTT TTC CTC GTT  Met Glu Ser Gly Xaa Gly Xaa Val Phe Leu Val  -15 -10	113
GCT CTT TTA AGA GGT GTC CAG TGT CAG GTG CAG ATT GTG CAG TCT GGG Ala Leu Leu Arg Gly Val Gln Cys Gln Val Gln Ile Val Gln Ser Gly -5 1 5	161
GGA GGC GTG GTC CAG CCT GGG AAG TCC CAG ACA CTC TCC TGT GTT ACC Gly Gly Val Val Gln Pro Gly Lys Ser Gln Thr Leu Ser Cys Val Thr 10 15 20	209
TAT GGA TTC AGA TTC GAT GAC TTT GGC TTC CAC TGG GTC CGC CAG GCT Tyr Gly Phe Arg Phe Asp Asp Phe Gly Phe His Trp Val Arg Gln Ala 25 30 35 40	257
CCA GGC AAG GGG CTG GAA TGG GTG GCA ATG ATA CGT TAT GAT GGA AGT Pro Gly Lys Gly Leu Glu Trp Val Ala Met Ile Arg Tyr Asp Gly Ser 45 50 55	305
AAT AAA TTC TAC TCA AAG TCT GTT CAG GGC CGA TTT CTC ATC TCC AGA Asn Lys Phe Tyr Ser Lys Ser Val Gln Gly Arg Phe Leu Ile Ser Arg 60 65 70	353
GAC AAT TCC AGA AAC CAA GTC TAT TTG AGT CTG AAC AGA CTG AGA GTC Asp Asn Ser Arg Asn Gln Val Tyr Leu Ser Leu Asn Arg Leu Arg Val 75 80 85	401
GAC GAC ACG GCT GTC TAT TAT Asp Asp Thr Ala Val Tyr Tyr 90 95	422

## (2) INFORMATION FOR SEQ ID NO: 127:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 366 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR

(ii)	MOLECULE	TYPE:	CDNA		

(sri)	ORIGINA	AL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Umbilical cord-

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 134..363
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..230 id AA009645

est

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 289..339
- (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9.3

seq LFTLLLLQSLLLG/CC

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

CAAAT	GATGT	ATTC	AGTGAA	TAAAA	SAATC	CCI	TTTA	TAA	AATC	TATT	TT	TCTTI	TAAAT	C 60	J
TTGGA	AAAAT	GTTGT	TTTAG	CTCAG	AGTGA	TTT	CAAA	.GTG	GAAT	GCAA	CA	GTAGI	rcaag:	A 12	٥
CTTGT	GTACT	ATAAA	ATCCTT	TTCTG	ATTCC	TTA	CAGA	TTT	GTAG	TGAT	'GA	GGTTI	'AGAT	T 18	0
TAATT	TTATA	TATGO	TKTAA	ATAAT'	IGTTA	AGC	KTAT	ATA	ACCI	GATO	TG	AATTO	CAGT	T 24	٥
GTTTG	CATKT	CCTCT	ratgaa	AACTT	CATTT	ATC	TAAT	'AAG	GAAG	TCAA			TGT Cys -15	·	7
				TT TTG eu Leu										34	5
				AT GGG sn Gly										36	6

# (2) INFORMATION FOR SEQ ID NO: 128:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 308 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia

· \*\*\* - \*\*\*

(ix) FEATU	T	'EA	. F	)	X	i	ĺ
------------	---	-----	-----	---	---	---	---

- (A) NAME/KEY: other
- (B) LOCATION: 43..97
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 1..55 id H30111

est

### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 18..95
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 9.3

seq FLLLVAGPRWVLS/QV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

AGTGCTTTCT GAGAGTC ATG GAC CTC CTG CAC AAG AAC ATG AAA CAC CTG  Met Asp Leu Leu His Lys Asn Met Lys His Leu  -25 -20	50
TGG TTC TTC CTC CTC GTG GCA GGT CCC AGA TGG GTC CTG TCC CAA  Trp Phe Phe Leu Leu Val Ala Gly Pro Arg Trp Val Leu Ser Gln -15 -10 -5 1	98 :
GTG CGG CTG GAA CAG TGG GGC TCT GGA CTA GTG AAG TCT TCC GAA ACG Val Arg Leu Glu Gln Trp Gly Ser Gly Leu Val Lys Ser Ser Glu Thr 5 10 15	146
CTG TCC CTC ACC TGC GCT GTC TAT GGT GGA TCC GCC ATC AGT GAC TAC Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Ala Ile Ser Asp Tyr 20 25 30	
TGG GCT TGG ATC CGT CAA TTC CCA GGA AAG GGA GTG GAG TGG ATC GGT Trp Ala Trp Ile Arg Gln Phe Pro Gly Lys Gly Val Glu Trp Ile Gly 35 40 45	

GAA ATC AAT CAC AGT GGC GCC ACC CAC TAT ATC CGT CCC TCA GGG GTC

Glu Ile Asn His Ser Gly Ala Thr His Tyr Ile Arg Pro Ser Gly Val

50 55 60 65

GAG TCG CCA TCT CCG CTG Glu Ser Pro Ser Pro Leu 70 308

### (2) INFORMATION FOR SEQ ID NO: 129:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 355 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens

يست عداسا

(F) TISSUE TYPE: Lymph ganglia

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 41..237
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..197

id R68856

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 236..354
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97.

region 197..315

id R68856

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 44..354
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..311

id T87538

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 43..331
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 2..290

id W95563

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 62..237
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 1..176

id H67429

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 236..354
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 176..294

id H67429

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 65..354
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..290 id AA046628 est

(ix)	FEATURE

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 125..277
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 8.1

seq VCLCGTFCFPCLG/CQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:

AAAC	TTAC	CTC	CTCCC	CTTI	C AC	GTAF	RTTTI	CAT	TTGT	GGT	GAGA	TTCI	CT (	CCAI	RGCCA	60
AAGA	CATI	TC C	CTGCI	CGG	AA CC	TTGT	TTAC	TA	ATTTC	CAC	TGCT	TTT	AG C	CCC1	rgcac1	120
gaaa			Ala					l Val					Pro		A GTC / Val	169
									AAC Asn							217
									CTC Leu							265
									GAT Asp							313
									CTC Leu							355

# (2) INFORMATION FOR SEQ ID NO: 130:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 229 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

## (ii) MOLECULE TYPE: CDNA

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymphocytes

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 177..229
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90 region 1..53 id N41594

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(A) ORGANISM: Homo Sapiens(F) TISSUE TYPE: Lymph ganglia

(C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94

(C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94

region 82..254 id AA075901

region 1..194

(A) NAME/KEY: other(B) LOCATION: 87..259

(A) NAME/KEY: other (B) LOCATION: 66..259

(ix) FEATURE:

(ix) FEATURE:

est

(B) LOCATION: 74127	
(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 7.7 seq LLLLPVLGLLVSS/KT	. • •
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:	
AAAGAAAGAG CTGCSGTGCA GGAATTCGTG TGCCGGATTT GGTTAGCTGA GCCCACCGAG	60
AGGCGCCTGC AGG ATG AAA GCT CTC TGT CTC CTC CTC CTC CTC CTG  Met Lys Ala Leu Cys Leu Leu Leu Pro Val Leu  -15  -10	109
GGG CTG TTG GTG TCT AGC AAG ACC CTG TGC TCC ATG GAA GAA GCC ATC Gly Leu Leu Val Ser Ser Lys Thr Leu Cys Ser Met Glu Glu Ala Ile -5 5 10	157
AAT GAG AGG ATC CAG GAG GTC GCC GGC TCC CTA ATA TTT AGG GCA ATA Asn Glu Arg Ile Gln Glu Val Ala Gly Ser Leu Ile Phe Arg Ala Ile 15 20 25	205
AGC AGC ATT GGC CGA GGG AGC GAG Ser Ser Ile Gly Arg Gly Ser Glu 30	229
(2) INFORMATION FOR SEQ ID NO: 131:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 265 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
(vi) ORIGINAL SOURCE:	

Water The

id R55519 est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 66..259

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 2..195 id H25630

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 67..259

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 3..195

id H43485

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 78..259

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 1..182

id H80718

est

### (ix) FEATURE:

Thr His Gly

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 89..151

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 6.6

seq LLXIVGLXLPTXG/QX

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

		•												
ACCTGG	CYSB M	CMCTC	CGCC T	GGNC	CAGO	AKC	CACC	GCH	GCGT	CCCI	CT C	TCCP	CGAGG	60
CTGCCG	GCTT A	GGACC	CCCA K	CTCC		let S	CG C Ser E -20				Arg I			112
			GTT GGC Val Gly											160
			ICC AG1 Ser Sei											208
			CGA GCC Arg Ala 2	Pro					Thr					256
ACC C	AC GGG												•	265

-

### (2) INFORMATION FOR SEQ ID NO: 132:

### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 314 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 79..240
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96

region 28..189 id AA122029

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 82..267
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 26..211 id HUML1833

IU n

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 148..275
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 1..128

id AA158721

est

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 147..209
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.2

seq FLVSNMLLAEAYG/SG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

ALGITICIAAA GAGAGGCIGK WIACCAKAAC AGCATAACAA GGGCAGGICI GACIGCAAGG 60

CTGTGGACTG GGAGGCAGAG CCGCCGCCAA GGGGGCCTCG GTTAARCACT GGTCGTTCAA 120

TCACCTGCAA GACGAAGGAG GCAAGG ATG CTG TTG GCC TGG GTA CAA GCA TTC 173

Met Leu Leu Ala Trp Val Gln Ala Phe

0 -15

CTC GTC AGC AAC ATG CTC CTA GCA GAA GCC TAT GGA TCT GGA GGC TGT
Leu Val Ser Asn Met Leu Leu Ala Glu Ala Tyr Gly Ser Gly Gly Cys
-10

TTC TGG GAC AAC GGC CAC CTG TAC CGG GAG GAC CAG ACC TCC CCC GCG
Phe Trp Asp Asn Gly His Leu Tyr Arg Glu Asp Gln Thr Ser Pro Ala
5

CCG GGC CTC CGC TGC CTC AAC TGG CTG GAC GCG CAG AAC GGG CTG
Pro Gly Leu Arg Cys Leu Asn Trp Leu Asp Ala Gln Asn Gly Leu
25

30

221

222

## (2) INFORMATION FOR SEQ ID NO: 133:

. ....

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 421 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 67..123
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98 region 1..57 id H30111 est
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 41..137
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 90 region 1..97 id T27715 est
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 43..137
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 91

region 2..96 id T27727

00+

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 136..213
  - (C) IDENTIFICATION METHOD: blastn
  - (D; OTHER INFORMATION: identity 92 region 93..170

\*\*\*\*\*\*\*\*\*\*\*

id T27727 est

1	4	X.	١ ١	 Δ	T	TT'	RE	٠.
L	_	Λ.		 •		u.		

(A) NAME/KEY: other(B) LOCATION: 98..137

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 90

region 1..40 id H43753

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 44..137

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 92

region 4..97 id T28164

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 26..211

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.8

seq LXLTCSVSGGSIS/RT

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

AATTCANNTC CAACTCATAA GGGAA		AGT CGT GGA CCT CCT 52 Ser Arg Gly Pro Pro -55
GTG CAA GAA CAT GAA GCA CCT Val Gln Glu His Glu Ala Pro -50		
TCC CAG ATG GGT CCT GTC CCA Ser Gln Met Gly Pro Val Pro -35		
GGA VTG GTG AAG CCT TTG GAG Gly Xaa Val Lys Pro Leu Glu -20 -15	Thr Leu Xaa Leu	
GGT GGC TCG ATC AGT AGG ACC Gly Gly Ser Ile Ser Arg Thr -5		
CCC CCA GGG AAG GGA CTG GAG Pro Pro Gly Lys Gly Leu Glu 15		
AGC ACC TAC TAC AAC CCG TCC Ser Thr Tyr Tyr Asn Pro Ser 30		
GAC ACG TCC AAG AAC CAG GTG Asp Thr Ser Lys Asn Gln Val		

PCT/IB98/01237

55

45

---

GCG GAC ACG GCC GTA TAT CAC TGT GCG AGA GGG Ala Asp Thr Ala Val Tyr His Cys Ala Arg Gly 60 65 70

421

#### (2) INFORMATION FOR SEQ ID NO: 134:

#### (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 431 base pairs

50

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

## (ii) MOLECULE TYPE: CDNA

### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 220..343
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..124 id N57208

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 329..431
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93

region 111..213

id N57208

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 329..431
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 55..157

id R94133

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 276..343
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 1..68

id R94133

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 344..431

---

(C)	IDENT	IFICATION	METH	DD:	blas	tn	Ł
(D)	OTHER	INFORMAT:	ION:	ide	entit	y	93
				re	gion	1.	.8
				id	AA11	09	14
				es	t		

## (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 21..344

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.3

seq ACMTLTASPGVFP/SL

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

AAACAACTCC GGAAAGTACA ATG ACC AGC GGG CAG GCC CGA GCT TCC WYC CAG Met Thr Ser Gly Gln Ala Arg Ala Ser Xaa Gln -105 -100	53 <sup>.</sup>
TCC CCC CAG GCC CTG GAG GAC TCG GGC CCG GTG AAT ATC TCA GTC TCA Ser Pro Gln Ala Leu Glu Asp Ser Gly Pro Val Asn Ile Ser Val Ser -95 -85	101
ATC ACC CTA ACC CTG GAC CCA CTG AAA CCC TTC GGA GGG TAT TCC CGC  Ile Thr Leu Thr Leu Asp Pro Leu Lys Pro Phe Gly Gly Tyr Ser Arg -80 -75 -70	149
AAC GTC ACC CAT CTG TAC TCA ACC ATC TTA GGG CAT CAG ATT GGA CTT Asn Val Thr His Leu Tyr Ser Thr Ile Leu Gly His Gln Ile Gly Leu -65 -50 -50	197
TCA GGC AGG GAA GCC CAC GAG GAG ATA AAC ATC ACC TTC ACC CTG CCT Ser Gly Arg Glu Ala His Glu Glu Ile Asn Ile Thr Phe Thr Leu Pro -45 -40 -35	245
ACA GCG TGG AGC TCA GAT GAC TGC GCC CTC CAC GGT CAC TGT GAG CAG Thr Ala Trp Ser Ser Asp Asp Cys Ala Leu His Gly His Cys Glu Gln -30 -25 -20	293
GTG GTA TTC ACA GCC TGC ATG ACC CTC ACG GCC AGC CCT GGG GTG TTC Val Val Phe Thr Ala Cys Met Thr Leu Thr Ala Ser Pro Gly Val Phe -15 -5	341
CCG TCA CTG TAC AGC CAC CGC ACT GTG TTC CTG ACA CGT ACA GCA ACG Pro Ser Leu Tyr Ser His Arg Thr Val Phe Leu Thr Arg Thr Ala Thr 1 5 10 15	389
CCA CGC TCT GGT ACA AGA TCT TCA CAA CTG CCA GAG ATG CCA Pro Arg Ser Gly Thr Arg Ser Ser Gln Leu Pro Glu Met Pro 20 25	431

# (2) INFORMATION FOR SEQ ID NO: 135:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 144 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (C) TOPOLOGY: LINEAR

· MASINE THE

(ii)	MOLECULE	TYPE:	CDNA
------	----------	-------	------

#### (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Lymph ganglia

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 111..142
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96 region 2..33 id R30650

.

# (ix) FEATURE:

(A) NAME/KEY: sig peptide

- (B) LOCATION: 1..63
- (C) IDENTIFICATION METHOD: Von Heijne matrix

est

(D) OTHER INFORMATION: score 5.1

seq LLLKIWLLQRPES/QE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

ATG CTG GGA GGT GAC CAT AGG GCT CTG CTT TTA AAG ATA TGG CTG CTT

Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu

-20 -15 -10

CAA AGG CCA GAG TCA CAG GAA GGA CTT CTT CCA GGG AGA TTA GTG GTG

Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val

-5

1

5
10

ATG GAG AGG AGA GTT AAA AAT GAC CTC ATG TCC TTC TTG TCC ACG GCG

Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Ala

15 20 25

# (2) INFORMATION FOR SEQ ID NO: 136:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 301 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 248..300
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 1..53 id HSC1XE021

est

(ix)	FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 134220  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.6  seq SLMSLLDESSCQA/VG
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 136:
AAGCGTCCCT	TTGTTGTGAA GGCGCCGGGG CCTAGCGCTA TGCCTGCGGC GGAGACTGCA 60
TCAGGCTCTC	GTCCTCGGGC TCCACCCAGG GAGCTGTGCC CAGACAGCAG AAGGGAAGGA 120
TGTCACTTCT	GAG ATG AGG TTC AGA AAG GCC TGG GCT CCT GTC CTG GCT  Met Arg Phe Arg Lys Ala Trp Ala Pro Val Leu Ala  -25  -20
	C CAC TCC CTG ATG AGC TTG CTG GAT GAA AGC TCC TGT CAG  r His Ser Leu Met Ser Leu Leu Asp Glu Ser Ser Cys Gln  -10  -5
	G CGT CCT GTG GAG AAA CTG GCA AGA AAC TGG TGG GGG CCC 265 y Arg Pro Val Glu Lys Leu Ala Arg Asn Trp Trp Gly Pro 5 10 15
	T ATA GCC AGC AAG GAA CTG AAC CCA GCG  o Ile Ala Ser Lys Glu Leu Asn Pro Ala 20 25
(2) INFORM	ATION FOR SEQ ID NO: 137:
(i) -	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 377 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR
	MOLECULE TYPE: CDNA
(41)	ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Lymph ganglia

#### (E) LOC

(ix) FEATURE:

- (A) NAME/KEY: other
  - (2) LOCATION: 95..377
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 1..293 id AA148067 est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 133...327
- (C) IDENTIFICATION METHOD: blastn

107 (D) OTHER INFORMATION: identity 98 region 58..252 id AA129289 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 75..136 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 171..242

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98 region 263..334

id R56463 est ·

region 1..62 id AA129289

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 239..284

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 332..377 id R56463

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 145..180

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 91

region 236..271

id R56463

est

# (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 63..308

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 4.4

seq NLPHLQVVGLTWG/HI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

AACTTCCGGT CGCGCCASCG CCCGTTGCCA GTTCTGCGCG TGTCCTGCAT CTCCAGTATG

107 GA ATG TAT GTD TGG CCC TGT GCT GTG GTC CTG GCC CAG TAC CTT TGG Met Tyr Val Trp Pro Cys Ala Val Val Leu Ala Gln Tyr Leu Trp -75

TTT CAC AGA AGA TCT CTG CCA GGC AAG GCC ATC TTA GAG ATT GGA GCT Phe His Arg Arg Ser Leu Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala -60 -65

GGA GTG AGC CTT CCA GGA ATT TTG GCT GCC AAA TGT GGT GCA GAA GTA

Gly Val Ser Leu Pro Gly Ile Leu Ala Ala Lys Cys Gly Ala Glu Val

-50

ATA CTG TCA GAC AGC TCA GAA CTG CCT CAC TGT CTG GAA GTC TGT CGG

Ile Leu Ser Asp Ser Ser Glu Leu Pro His Cys Leu Glu Val Cys Arg

-35

CAA AGC TGC CAA ATG AAT AAC CTG CCA CAT CTG CAG GTG GTA GGA CTA

Gln Ser Cys Gln Met Asn Asn Leu Pro His Leu Gln Val Val Gly Leu

-15

ACA TGG GGT CAT ATA TCT TGG GAT CTT CTG GCT CTA CCA CCA CAA GAT

347

Thr Trp Gly His Ile Ser Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp

1 5 10

ATT ATC CTT GCA TCT GAT GTG TTC TTT GAA 377

ATT ATC CTT GCA TCT GAT GTG TTC TTT GAA

Ile Ile Leu Ala Ser Asp Val Phe Phe Glu
15 20

# (2) INFORMATION FOR SEQ ID NO: 138:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 380 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 308..380
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98 region 29..101

id W52747

est

(ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 265..294
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93

region 1..30 id W52747

est

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 3..170
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.4 seq LWKLALQSSSCLS/LF

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

let I			3ln X		ATG Met	Pro				47
					TTT Phe		Phe			95
 	 	 			CTG Leu -15	Asn				143
					TTT Phe					191
					GTA Val			Arg		239
 					AAG Lys		Ala			287
					AAG Lys 50	Xaa				335
		Thr			CAA Glr					380

# (2) INFORMATION FOR SEQ ID NO: 139:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 214 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 104..213
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98 region 2..111 id T11539 est
- (ix) FEATURE:

120

169

214

-10

. ...

-			
WO 99/06	553 110	PC1	
	(A) NAME/KEY: sig_peptide		
	(B) LOCATION: 134205		
	(C) IDENTIFICATION METHOD: Von Heijne matrix		
	(D) OTHER INFORMATION: score 3.9 seq GVCLSVPSLPSIS/RP		
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 139:		
ACACAGTGAT	GTAGAGCTTT GGCTCTTTGT AACCAGGAGT TCGATAGGAA GACAACTT	TG	
AAAAAGCACT	TTGTGACTGG CAGGGTGCCA TGCAGCCTCA GCTGTTCATT TCCAAGGG	TC	
ATCCATTTAC	AGG ATG AAT GCT CAA GCC TCT TCC TCC CGG TGC CAT GGA		

Met Asn Ala Gln Ala Ser Ser Ser Arg Cys His Gly

-20

GTC TGC CTG TCA GTC CCC TCC TTG CCC AGC ATC TCC CGC CCG CCG

Val Cys Leu Ser Val Pro Ser Leu Pro Ser Ile Ser Arg Pro Pro -5

(2) INFORMATION FOR SEQ ID NO: 140:

# (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 485 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 263..411
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 155..303 id AA005338

est ·

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 110..208
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95 region 1..99 id AA005338

- (A) NAME/KEY: other
- (B) LOCATION: 409..469
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95 region 302..362

id AA005338 est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 206..250
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 98..142 id AA005338

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 299..446
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 192..339

id AA005431

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 110..208
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 1..99 id AA005431

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 206..250
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 98..142

id AA005431

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 263..300
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 155..192

id AA005431

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 263..433
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 175..345

id W78855

est

- (A) NAME/KEY: other
- (B) LOCATION: 89..250
- (C) IDENTIFICATION METHOD: blastn

w-E--

(D) OTHER INFORMATION: identity 99

region 1..162 id W78855

#### (ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 89..250

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 2..163 id H52413

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 263..400

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 91

region 176..313

id H52413

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 263..389

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 5..131 id AA057872

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 375..470

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 118..213

id AA057872

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 264..464

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 3.8

seq QVLDSVLVGPVPA/ER

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

ATGAACTCGG GTGCAGCCAA TCGAGGGCAA CGCTGCTACT TATCAGAGCA GAATGGGCTG. TAGTTTAGTG AAATAGGAAA GCTGCAACAC ACTGTGGAGT GCTCCCGTGT AAATAATAAG AGGAAAAAG TTTCTCAAGT CGCCGCTGCA CGACGTCTGG CCGGCGCTGG AGCGGGGGTC 180 TGCGCTCTCC CGAGCGGCCG CGCGCTGGAC TTTATTGTGC CGCAACCAGC CCCAGTTCCC ATTGTTTGTG TTTTTTCAA AAT ATG GCA AAG GTT CAG GTG AAC AAT GTA GTG Met Ala Lys Val Gln Val Asn Asn Val Val

· water

-65

GTG CTG GAT AAC CCT TCT CCT TTC TAC AAC CCG TTC CAG TTC GAG ATC 341 Val Leu Asp Asn Pro Ser Pro Phe Tyr Asn Pro Phe Gln Phe Glu Ile ACC TTC GAG TGC ATC GAG GAC CTG TCT GAA GAC TTG GAA TGG AAA ATT 389 Thr Phe Glu Cys Ile Glu Asp Leu Ser Glu Asp Leu Glu Trp Lys Ile ATC TAT GTG GGC TCT GCA GAA AGT GAA GAA TAC GAT CAA GTT TTA GAC 437 Ile Tyr Val Gly Ser Ala Glu Ser Glu Glu Tyr Asp Gln Val Leu Asp -20 -15 -25 TCT GTT TTA GTG GGT CCT GTT CCC GCA GAA AGG CAT ATG TTT GTA TTT 485 Ser Val Leu Val Gly Pro Val Pro Ala Glu Arg His Met Phe Val Phe ~5 1

#### (2) INFORMATION FOR SEQ ID NO: 141:

# (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 169 base pairs
- (B) TYPE: NUCLEIC ACID
- (C): STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymphocytes

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 58..160
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 48..150 id AA037680 est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 58..122
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 31..95 id W81645

est

- (A) NAME/KEY: other
- (B) LOCATION: 121..170
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98 region 93..142 id W81645 est

l i x	١.	FEATURE:	
ιıx	1	FEATURE:	

(A) NAME/KEY: other
(B) LOCATION: 65..122

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 7..64 id W06951

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 121..170

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 62..111 id W06951

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 59..168

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 90

region 1..110 id AA034702

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 56..118

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 3.7

seq ETCALASHSGSSG/SK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

AAGCCTTCCG CCKTCCCCAA GCCAACGTCT CCGCCGTCGG CTCCGCGGCG CCGCC ATG
Met

GCC GAC GTG GAA GAC GGA GAG GAA ACC TGC GCC CTG GCC TCT CAC TCC

Ala Asp Val Glu Asp Gly Glu Glu Thr Cys Ala Leu Ala Ser His Ser

GGG AGC TCA GGC TCC AAG TCG GGA GGC GAC AAG ATG TTC TCC CTC AAG
Gly Ser Ser Gly Ser Lys Ser Gly Gly Asp Lys Met Phe Ser Leu Lys

1 bys ser GIY GIY ASP bys het the ser bed 1 10

AAG TGG AAC GCG GTG Lys Trp Asn Ala Val 169

15

### (2) INFORMATION FOR SEQ ID NO: 142:

# (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 141 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

· •

1111	MOLECULE	TYPE .	CDNA
LLLI	PIODECULE	1155.	CDIM

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 70..114

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 231..275

id AA130776

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 88..139

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 1..52 id AA121716

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 70..112

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 167..209

id AA146672

est

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 76..117

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 3.5

seq WTCLLGDCGPPEA/FT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

ACWMTTCCCT CTGTTGGAGC TCAGAACATG ACACTCCAAA ACATGGCACC TTGGTAATTA 60

CGAAAACAGC AGAAA ATG TGG ACA TGC TTA CTC GGG GAT TGT GGC CCA CCA 111
Met Trp Thr Cys Leu Leu Gly Asp Cys Gly Pro Pro

-10

GAA GCA TTT ACT TCC TAC CAA CCC CCC AGG Glu Ala Phe Thr Ser Tyr Gln Pro Pro Arg 141

(2) INFORMATION FOR SEQ ID NO: 143:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 247 base pairs

(B) TYPE: NUCLEIC ACID

	(C)	STRA	NDEDN	ESS:	DOUBLE
	(D)	TOPO	DLOGY:	LIN	EAR
(ii)	MOLE	CULE	TYPE:	CDN	A
1001	OPTG	TNAT	SOURC	r.	

# (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens(F) TISSUE TYPE: Lymph ganglia

# (ix) FEATURE:

- (A) NAME/KEY: other
  (B) LOCATION: 2..56
- (C) IDENTIFICATION METHOD: blastn
  (D) OTHER INFORMATION: identity 90
  region 10..64

id R86288 est

# (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 38..94

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 11.7 seq VFCLLAVAPGAHS/QV

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

ATCT	CTAC	AG A	ACCO	TCT	SA GA	AGGA	lagt1	CTI	CACC			ASG Xaa	55
GTC Val											CAG Gln 1		103
											TCA Ser		151
											TAT Tyr		199
											GGA Gly		247

#### (2) INFORMATION FOR SEQ ID NO: 144:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 307 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Umbilical cord

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 117..250

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 17..150

id R28399

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 240..278

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 92

region 141..179

id R28399

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (179..305)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: |identity 99

region 59..185

id R07794

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(149..184)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 181..216

id R07794

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 187..305

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 19..137

id H84735

est.

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 195..234

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 250..289

id R85011

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 240..278

(C) IDENTIFICATION METHOD: blastn

and the same		·	
WO 99/06553		118	PCT/IB98/01
(D)	OTHER INFORMATION:	identity 94 region 297335 id R85011 est	
(day) PERM	nne.	•	•
(B) (C)	NAME/KEY: other LOCATION: 195250 IDENTIFICATION METH OTHER INFORMATION:	OD: blastn identity 94 region 246301 id H52765 est	
(ix) FEAT	URE:		
(A) (B) (C)	NAME/KEY: sig_pepti LOCATION: 83181	OD: Von Heijne matrix	
(xi) SEQU	ENCE DESCRIPTION: SE	Q ID NO: 144:	•
AAACAGCTTC CCCT	AGCACA GCACAGACTA CA	AGACAGGGG AGCCTCTGGG G	CTGCAGACA 60
CTGCAGACGG ACGG		AC AGC TGG AGG CTT GGC sn Ser Trp Arg Leu Gly -30	
	Ala Gly Gln Ser Gl	CTG CTA GTG TCG CTG Leu Leu Val Ser Leu -10	
		A GAC GTG GCT GCC CCA r Asp Val Ala Ala Pro 5	
		C GAC ACC TTG GCG GGG n Asp Thr Leu Ala Gly 20	
		G CCT CTA GGC CAG TTC n Pro Leu Gly Gln Phe 35	
CGG Arg	· -		307
(2) INFORMATION	N FOR SEQ ID NO: 145	:	

# (2) INFO

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 291 base pairs
    (B) TYPE: NUCLEIC ACID

  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL	SOURCE:
---------------	---------

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 13..66
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 3..56

id H30111

est

# (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION:  $7..\overline{63}$
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 10.9

seq FLLLVAAPRWVLS/QV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

AAGAAC	ATG A	ARA	CAC	CTG	TSG	TTC	TTC	CTC	CTG	CTG	GTG	GCA	GCT	CCC	48
	Met 2	Xaa	His	Leu	Xaa	Phe	Phe	Leu	Leu	Leu	Val	Ala	Ala	Pro	
•					-15					-10	i				

AGA TGG GTC CTG TCC CAG GTG CTA CTA CAG GAG TCG GGC CCT GAA CTG
Arg Trp Val Leu Ser Gln Val Leu Leu Gln Glu Ser Gly Pro Glu Leu
-5 1 5 10

GTG AAG CCT TCA SAG ACC CTG TCC CTC ACC TGM GCT GTC TCT GGT GGC

Val Lys Pro Ser Xaa Thr Leu Ser Leu Thr Xaa Ala Val Ser Gly Gly

15

20
25

TCC ATC AGC GGT GGT CCT TAC TAT TGG AAC TGG GTC MGC CAG CAC CCA 192
Ser Ile Ser Gly Gly Pro Tyr Tyr Trp Asn Trp Val Xaa Gln His Pro
30 35 40

GGG AAG GGC CTG GAR WGG ATT GGC AAC ATC TAT TAC AAT GGG AGC ACC

Gly Lys Gly Leu Glu Xaa Ile Gly Asn Ile Tyr Tyr Asn Gly Ser Thr

45

50

55

TTC DHA RAA CCC GTC CCT CAA GAS TCG NCT TAT CAT ATC GYY AGA CGC

Phe Xaa Xaa Pro Val Pro Gln Xaa Ser Xaa Tyr His Ile Xaa Arg Arg

60 65 70 75

AGG 291 Arg

#### (2) INFORMATION FOR SEQ ID NO: 146:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 326 base pairs
  - (E) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MCLECULE TYPE: CDNA

(vi) ORIGINAL	SOURCE:
---------------	---------

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Lymph ganglia

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 205..321

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 107..223

id W05822

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 100..210

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 1..111 id W05822

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (218:..248)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 90

region 105..135 id AA135917

# (ix) FEATURE:

(A) NAME/KEY: sig peptide

(B) LOCATION: 72..155

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 9.6

seq LLTLLLGLTEVAG/EE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

#### AGTCTTCBSG CAGGGCCTGA CATCTCCCCA GAACAGACGT TTGAACAGAG CAGGCTTCTG 60

AGGTCTCCAA A ATG CCT GTC CCA GCC TCC TGG CCC CAT CCT CCT GGT CCT 110 Met Pro Val Pro Ala Ser Trp Pro His Pro Pro Gly Pro -25

-20

TTC CTG CTT CTG ACT CTA CTG CTR GGA CTT ACA GAA GTG GCA GGT GAG 158 Phe Leu Leu Thr Leu Leu Gly Leu Thr Glu Val Ala Gly Glu -15

GAR GAG CTA CAG ATG ATT CAG CCT GAG AAG CTC CTG TTG GTC ACA GTT Glu Glu Leu Gln Met Ile Gln Pro Glu Lys Leu Leu Val Thr Val 5 10

GGA AAG ACA GCC ACT CTG CAC TGC ACT GTG ACC TCC CTG CTT CCC GTG Gly Lys Thr Ala Thr Leu His Cys Thr Val Thr Ser Leu Leu Pro Val 20 25

GGA CCC GTC CTG TGG TTC AGA GGA GTT GGA CCA GGC CGG GAA TTA ATC

Gly Pro Val Leu Trp Phe Arg Gly Val Gly Pro Gly Arg Glu Leu Ile 35 40 45

TAC AAT CAA AAA GAA GGC CTA MNB Tyr Asn Gln Lys Glu Gly Leu Xaa 50 55 326

#### (2) INFORMATION FOR SEQ ID NO: 147:

#### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 330 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Umbilical cord

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 70..216
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 68..214 id W01897

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 4..56
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 1..53 id W01897 est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 237..273
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 238..274 id W01897

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 177..331
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99 region 1..155

id H87389

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

- To -

(B)	LOCATION	l: 2	17.	.261
-----	----------	------	-----	------

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 9.6

seq EYVLLLFLALCSA/KP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:

AAGTTTATTC CAGTATCACC CAGGGTGCAG CCACACCAGG ACTGTGTTGA AGGGTGTTTT TTTTCTTTTA AATGTAATAC CTCCTCATCT TTTCTTCTTA CACAGTGTCT GAGAACATTT 120 ACATTATAGA TAAGTAGTAC ATGGTGGATA ACTTCTACTT TTAGGAGGAC TACTCTCTC TGACAGTCCT AGACTGGTCT TCTACACTAA GACACC ATG AAG GAG TAT GTG CTC Met Lys Glu Tyr Val Leu -15 CTA TTA TTC CTG GCT TTG TGC TCT GCC AAA CCC TTC TTT AGC CCT TCA 282 Leu Leu Phe Leu Ala Leu Cys Ser Ala Lys Pro Phe Phe Ser Pro Ser -5 1 CAC ATC GCA CTG AAG AAT ATG ATG CTG AAG GAT ATG GAA GAC ACA GAG 330

His Ile Ala Leu Lys Asn Met Met Leu Lys Asp Met Glu Asp Thr Glu

# (2) INFORMATION FOR SEQ ID NO: 148:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 143 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 22..143
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95

region 1..122 id AA027314

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 51..143
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95 region 29..121

id AA149456

est

WO 99/06553	:	123	PCT/IB98/012
(B) (C)	NAME/KEY: other LOCATION: 69143 IDENTIFICATION METHO OTHER INFORMATION:		
(B) (C)	URE: NAME/KEY: other LOCATION: 3375 IDENTIFICATION METHO OTHER INFORMATION:	DD: blastn identity 100 region 143 id W17274 est	
(B) (C) (D)	URE:  NAME/KEY: sig_peptic LOCATION: 2777 IDENTIFICATION METHO OTHER INFORMATION:  ENCE DESCRIPTION: SEC	DD: Von Heijne matrix score 9.3 seq LALSLLILVLAFG/IP	
ACTCTTACTC ACCC		T CAG TCA CTG GCT CTG AG a Gln Ser Leu Ala Leu Se -15 -1	r Leu
	Leu Ala Phe Gly Ile	CCC AGG ACC CAA GGC AGT Pro Arg Thr Gln Gly Ser 5	
	GAC TGT TGC CTC AAG Asp Cys Cys Leu Lys 15		143
(i) SEQUE (A) (B) (C) (D)	FOR SEQ ID NO: 149: CNCE CHARACTERISTICS: LENGTH: 305 base partype: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR CULE TYPE: CDNA		

# (2) IN

# (7i) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

- (A) NAME/KEY: other
- (B) LOCATION: complement(228..303)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97 region 206..281

-

id N70479

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(77..112)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 403..438

id N70479

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(163..196)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 315..348

id N70479

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 57..107

(C) IDENTIFICATION METHOD: Von Heijne matrix

AACTTGCCAT TTCTCATAAC AGCGTCAGAG AGAAAGAACT GACTGAAACG TTTGAG ATG

(D) OTHER INFORMATION: score 8.2

seq LLLITAILAVAVG/FP

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:

										Met	
		GTT Val	 	 						 	107
		GTC Val									155
		GAA Glu	 	 			 	 		 	203
		CCA Pro 35	 	 				 	Trp	 	251
		TTT	 		Pro	-					299
CCG	ATG										305

Pro Met 65

(i) S	EQUENCE CHARAC (A) LENGTH: 3 (B) TYPE: NUC (C) STRANDEDN (D) TOPOLOGY:	323 base pai CLEIC ACID NESS: DOUBLE				•	
(ii)	MOLECULE TYPE	: CDNA					
•	ORIGINAL SOURG (A) ORGANISM: (F) TISSUE TY	Homo Sapie					
	FEATURE: (A) NAME/KEY: (B) LOCATION: (C) IDENTIFIC (D) OTHER INE	complement CATION METHO FORMATION:	D: blast	n 95 22281	4		
(ix)	FEATURE: (A) NAME/KEY (B) LOCATION (C) IDENTIFIC (D) OTHER IN	complement CATION METHO		n 94 03438		i. :	
(ix)	FEATURE: (A) NAME/KEY (B) LOCATION (C) IDENTIFIC (D) OTHER IN	: complement CATION METHO	DD: blast	n 94 15348			
(ix)	FEATURE: (A) NAME/KEY (B) LOCATION (C) IDENTIFI (D) OTHER IN	: 90140 CATION METHO		2			
(xi)	SEQUENCE DESC	RIPTION: SE	Q ID NO:	150:			
AATATRARAC	AGCTACAATA TT	CCAGGGCC AR	TCACTTGC	CATTTCTC	CAT AACAC	SCGTCA 60	)
GAGAGAAAGA	ACTGACTGAR AC		AAG AAA Lys Lys -15				3
	C TTG GCA GTG e Leu Ala Val -5						1

GAR DGA GAA AAA AGA AGT ATC AGT GAC AGC GAT GAA TTA GCT TCA GGR

Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly
10 15 20

WTT TTT GTG TTC CCT TAC CCA TAT CCA TTT CGC CCA CTT CCA CCA ATT
Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile
25 30 35

CCA TTT CCA AGA TTT CCA TGG TTT AGA CGT AAW TTT CCK ATT CCA ATA 305
Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Xaa Phe Pro Ile Pro Ile
40 45 50 55

CCT GAA TCT GCC CCT GGG Pro Glu Ser Ala Pro Gly 60 323

#### (2) INFORMATION FOR SEQ ID NO: 151:

#### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 302 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Placenta

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 130..267
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96 region 104..241 id T58582

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 28..129
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 1..102

id T58582

. est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 18..270
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 1..253

id C18397

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 97..300

O 99/06553		127
(C)	IDENTIFICATION MET	IOD: blastn
(D)	OTHER INFORMATION:	identity 99 region 2205 id R62763 est
(ix) FEAT	CURE:	
(A)	NAME/KEY: other	
(B)	LOCATION: 97300	•
(C)	IDENTIFICATION METH	IOD: blastn
(D)	OTHER INFORMATION:	identity 99 region 1204

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 150..203
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score-8.1

seq LFTAILAFSLAQS/FG

id R63635

est

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

AAG(	CTTC	CT	AGATO	CCC1	C C	ACTC	GTTI	CTC	CTCTT	TGC	AGG	AGCA	CCG (	GCAGO	CACCAG	60
TGT	STGAC	GGG	GAGC	AGGC	AG CO	GTC	CTAGO	CAC	STTC	CTTG	ATC	CTGC	CAG I	ACCAC	CCCAGC	120
ccc	CGGC	ACA	GAGC1	rgcto	CC A	CAGGO	CACC		AGG Arg			Leu				173
			GCC Ala							,					*	221
			GAG Glu 10	Glu												269
			TAC Tyr			-,										302

# (2) INFORMATION FOR SEQ ID NO: 152:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 416 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia

-

#### (ix) FEATURE:

- (A) NAME/KEY: other (B) LOCATION: 17..102
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 1..86 id H16140

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 15..47
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93

region 16..48

id H26913

est

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 42..92
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 7.9

seq VLLLGLLSHCTVS/VS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

AAGTCTGGGC CTAWGGAAGC	AGCACTGGTG	GTGCCTCAGC	С	ATG	GCC	TGG	ACC	GTT	56
				Met	Ala	Trp	Thr	Val	
						-15			

- CTC CTC CTC GGC CTC CTC TCT CAC TGC ACA GTG TCT GTG AGC TCC TAC

  Leu Leu Gly Leu Leu Ser His Cys Thr Val Ser Val Ser Ser Tyr

  -10

  -5
- GAA CTG ACT CAG CCA CCC TCA GTG TCA GTG GCC CCA GGA GAG ACG GCC 152
  Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Glu Thr Ala
  5 10 15 20
- ACC ATT TCC TGT GGG GCA AAC AAT GTT GGA AGA AAA AAT GTG CAG TGG
  Thr Ile Ser Cys Gly Ala Asn Asn Val Gly Arg Lys Asn Val Gln Trp
  25 30 35
- TAT CAG CAG AAG GCA GGC CAG GCC CCT GTG TTG GTC ATT TAC CAT GAT

  Tyr Gln Gln Lys Ala Gly Gln Ala Pro Val Leu Val Ile Tyr His Asp

  40

  45

  50
- GTC GAG CGG CCC TCG GGG ATT CCT GAG CGA TTC TCT GGC TCC AAC TCT 296
  Val Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser
  55 60 65
- GGG AGT CCG GCC AAA CTG ACC ATC AGC AGG GTC GAA GCC GGG GAT GAG
  Gly Ser Pro Ala Lys Leu Thr Ile Ser Arg Val Glu Ala Gly Asp Glu
  70 75 80
- GCC GAC TAT WAC TGT NAG GTG TGG GAC AGT GAC AGT GAT CAT ACG GTG
  Ala Asp Tyr Xaa Cys Xaa Val Trp Asp Ser Asp Ser Asp His Thr Val
  85 90 95 100

ATA TTC GGC GGC GGG ACC AAG CTG

-W-15-7-

Ile Phe Gly Gly Gly Thr Lys Leu 105

#### (2) INFORMATION FOR SEQ ID NO: 153:

#### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 519 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 166..454
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 91

region 87..375 id N23576

---

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 79..150
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 1..72

id N23576

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 445..520
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 367..442

id N23576

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (56..115)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 362..421

id W15210

est ·

- (A) NAME/KEY: other
- (B) LOCATION: complement(2..58)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96 region 418..474

id W15210 est

1	ix	١.	F	EΑ	т	11	R	Ē	•
		,	<b>E</b>			v	7	۰	

(A) NAME/KEY: other

(B) LOCATION: complement(2..118)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 18..134

id R07597

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 274..447

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 7.7

seq PXLLLQTLPASTX/XP

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

AAGTACCTTT TCAGTCTTGC CCCAGAGGTT CCCTCAATTT CAGCAGCACC GAGCGGTTTA	60
TAATTCATTC AGTTTTCCAG GCCAGGCAGC CCGCTATCCT TGGATGGCCT TTCCACGCAA	120
TAGCATCATG CACTTGAACC ACACARCATA BGAGAGGGNR GNNNNSTAAT TTSTTGGACT	180
TSSVTSTBCC GCCACAGCRS AACACAGGTC TGGGAGGGAT CCCTGTAGCA GGTATTCCAG	240
CGTCTTCAGG AAACAGTTTA GACTCTCTTC AAG ATG ACA ATC CTC CAC ACT GGS  Met Thr Ile Leu His Thr Gly  -55	294
KAA AAT CCC TTC AGG CCC TCA CAG AGA TGG ACG GCC CCA GCG CTC CTC Xaa Asn Pro Phe Arg Pro Ser Gln Arg Trp Thr Ala Pro Ala Leu Leu -50 -45	342
CAT CAC AGA CCC AMC ACA GBG CCC CCT TCA GKA CAC AGA TCC CGC TGC His His Arg Pro Xaa Thr Xaa Pro Pro Ser Xaa His Arg Ser Arg Cys -35 -30 -20	390
ACA GAG BYA GTT GGA ATC CCT RCS CTC CTC CTT CAR ACS CTT CCA GCT Thr Glu Xaa Val Gly Ile Pro Xaa Leu Leu Leu Gln Thr Leu Pro Ala -15 -10 -5	438
TCC ACT MCC CAS CCC CAG GCT TTC AGA CGG MCT TCA GAC CCC CCA GCA Ser Thr Xaa Xaa Pro Gln Ala Phe Arg Arg Xaa Ser Asp Pro Pro Ala 1 5 10	486
AAA CCC CCA CAG ATT TAC TAC AGA GTT CAA CAC Lys Pro Pro Gln Ile Tyr Tyr Arg Val Gln His 15 20	519

# (2) INFORMATION FOR SEQ ID NO: 154:

# (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 384 base pairs
- (B) TYPE: NUCLEIC ACID

(C)	STRANDEDNESS	: DOUBLE
(D)	TOPOLOGY: LI	NEAR

# (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens(F) TISSUE TYPE: Lymph ganglia

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 21..73
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92 region 4..56

id T28164 est

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 40..99
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 7.2

seq LLLLVAAPKXXLS/QV

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

ATAT	'ACT'I	TC I	GAGA	AGTBC	T GG	ACCI	CCTG	TGC	AAGA	M	AA C		54
					CTG Leu -10								102
					TCG Ser								150
					AGT Ser								198
					ATC Ile								246
					TAC Tyr 55					-	 		294
					CTA Leu								342
					ATG Met								384

#### (2) INFORMATION FOR SEQ ID NO: 155:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 248 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 69..194
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 1..126

id R65867

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 208..245
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

region 140..177

id R65867

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(208..245)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

region 194..231

id R22927

est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 120..182
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.9

seq LVCGSLGLSNVSG/IY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:

AATATTTATA TAAATATTAB YTATTAGTGA GTTGTTATTC ATCCTTTGGA TGCAAATTGT 60

AAATTAGGAA ACTATTTAT TACTGCTTTT TTGTGGTTAA ACACTTTATT TTAATATAA 119

ATG TTG AGT TAT TTT CTA TCC TCT TTG GTG TGC GGT AGT TTA GGT CTC 167

Met Leu Ser Tyr Phe Leu Ser Ser Leu Val Cys Gly Ser Leu Gly Leu
-20 -15 -10

AGT AAT GTT TCT GGT ATA TAT GAT TCC AAA AAA AAG CGA AAA ACA GGT 215

\*\*\* -E \*

Ser Asn Val Ser Gly Ile Tyr Asp Ser Lys Lys Lys Arg Lys Thr Gly
-5 1 5 10

GCT TTT AGG ACA CAA CTT TTC TGG GGA GTC GGG Ala Phe Arg Thr Gln Leu Phe Trp Gly Val Gly 15 248

#### (2) INFORMATION FOR SEQ ID NO: 156:

#### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 380 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 184..354
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99 region 172..342 id AA043042

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 68..185
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 55..172

id AA043042

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 12..52
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 1..41

id AA043042

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 68..277
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 57..266

id AA042861

est

#### (ix) FEATURE:

(A) NAME/KEY: other

----

- (B) LOCATION: 276..348
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 266..338 id AA042861

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 10..52
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 90

region 1..43 id AA042861

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 50..348
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 41..339

id R76970

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 19..52
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 11..44

id R76970

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 50..331
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 40..321

id AA042849

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 10..52
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 1..43

id AA042849

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 92..369
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 24..301

id H60916

est

(ix) FEAT	JRE:	:
-----------	------	---

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 210..335
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.4

seq ELPALALLHAGHA/EP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

AAGAGATCTG GGAACCCGGG AGCCGAGGTA ACGAACAGCT CGGTGGCAGG GCCTGACTGC	60
TGCGGAGGCC TCGGCAATAT TGATTTTAGA CAGGCAGACT TCTGCGTTAT GACCCGGCTG	120
CTGGGCTACG TGGACCCCCT GGATCCCAGC TTTGTGGCTG CCGTCATCAC CATCACCTTC	180
AATCCGCTCT ACTGGAATGT GGTTGCACG ATG GGA ACA CAA GAC CCG CAA GCT Met Gly Thr Gln Asp Pro Gln Ala -40 -35	233
GAG CAG GGC CTT CGG ATC CCC CTA CCT GGC CTG CTA CTC TCT AAG CAT Glu Gln Gly Leu Arg Ile Pro Leu Pro Gly Leu Leu Leu Ser Lys His -30 -25	281
CAC CAT CCT GCT CCT GAA CTT CCT GCG CTC GCA CTG CTT CAC GCA GGC His His Pro Ala Pro Glu Leu Pro Ala Leu Ala Leu Leu His Ala Gly -15 -5	329
CAT GCT GAG CCA GCC CAG GAT GGA GAG CCT GGA CAC CCC CGC GGC CCA His Ala Glu Pro Ala Gln Asp Gly Glu Pro Gly His Pro Arg Gly Pro 1 5 10	377
GGG Gly 15	380

# (2) INFORMATION FOR SEQ ID NO: 157:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 288 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 23..251
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96 region 78..306 id T87972

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 251..283
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 307..339

id T87972

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (36..283)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 89..336

id AA040027

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(68..283)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 81..296

id R82948

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (66..283)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 104..321

id H26425

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(27..60)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 329..362

id H26425

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (127..245)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 127..245

id T55847

id T55847

est

- (A) NAME/KEY: other
- (3) LOCATION: complement(68..131)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96 region 242..305

est

(ix)	FEATURE:
------	----------

- (A) NAME/KEY: other
- (B) EOCATION: complement(237..283)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 88..134

id T55847

est

# (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 61..159
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.3

seq SXXPLXSVQLXHA/QR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

ATA	LATAC	SAA . A	AAAA	AAA	T T	GTT	CCT	A GGT	TGA	AGGT	CTAP	\TTG/	ATA (	CGTTI	GACTT	60
	-					CTT Leu										108
						TTW Xaa										156
						GAT Asp						_	_			204
						CTT Leu										252
						GAT Asp										288

# (2) INFORMATION FOR SEQ ID NO: 158:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 294 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymphocytes
- (ix) FEATURE:
  - (A) NAME/KEY: other

(B) LOCATION: 2..210

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 19..227 id W04921

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 211..290

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 227..306

id W04921

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (23..203)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 260..440

id N70602

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (203..248)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 216..261

id N70602

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (251..290)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 175..214

id N70602 -

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 47..177

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 1..131

id W37690

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 211..290

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 165..244

id W37690

est

	1101	FEATURE	
1	1 1. X I	FEATURE	Ξ

(A) NAME/KEY: other

(B) LOCATION: 175..210

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 130..165

id W37690

est

#### (ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 46..184

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 1..139

id W70167

est:

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 228..290

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 183..245

id W70167

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 183..226

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 139..182

id W70167

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 217..279

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 6.1

seq LEMLTAFASHIRA/RD

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

ACCTTGGCTC GGCTTGGTCT GCGGCCTGTC AAACAGGTTC GGGTTCAGTT CTGTCCCTTC 60

GAGAAAAACG TGGAATCGAC GAGGACCTTC CTGCAGACGG TGAGCAGTGA GAAGGTCCGC 120

TCCACTAATC TCAACTGCTC AGTGATTGCG GACGTGAGGY ATGACGGCTC CGAGCCCTGC 180

GTGGACGTGC TGTTCGGAGA CGGGCATCGC CTGATT ATG CGC GGC GCT CAT CTC ATG CGC ATG ATG GIY Ala His Leu -20

AYC GCT CTG GAA ATG CTC ACC GCC TTC GCC TCC CAC ATC CGG GCC AGG 282

Xaa Ala Leu Glu Met Leu Thr Ala Phe Ala Ser His Ile Arg Ala Arg -15 -10 -5 1

GAY GCG GCA AGG

Asp Ala Ala Arg

# (2) INFORMATION FOR SEQ ID NO: 159:

# (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 288 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Umbilical cord

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(2..285)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 26..309

id H54590

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 107..285
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 78..256

id AA143123

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(169..285)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 320..436

id AA142922

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(119..168)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 436..485

id AA142922

est

- (A) NAME/KEY: other
- (B) LOCATION: 29..91
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93 region 2..64

id N88917 est

ĺ	ix	FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 83..140

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 55..112 id N88917

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 218..285

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 10..77 id AA013161

est

#### (ix) FEATURE:

(A) NAME/KEY: sig peptide

(B) LOCATION: 76..231

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 6.1

seq IILLIHTMQVCTT/HP

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

# AGTACCGATC CTCAGAGGAA GAGAAGAGAG TGACAGTCAT CAAAGCCCCG CATTACCCAG

GGATCGGGCC CGTGG ATG AAT CCG GAA TCC CCA CAG CAA TTA GAA CGA CAG 111 Met Asn Pro Glu Ser Pro Gln Gln Leu Glu Arg Gln -50

TCG ACC GGC CCA AGG ACT GGT ACA AGA CGA TGT TTA AGC AAA TTC ACA 159 Ser Thr Gly Pro Arg Thr Gly Thr Arg Arg Cys Leu Ser Lys Phe Thr -40

TGG TGC ACA AGC CGG ATG ATG ACA CAG ACA TGT ATA ATA CTC CTT ATA 207 Trp Cys Thr Ser Arg Met Met Thr Gln Thr Cys Ile Ile Leu Leu Ile -20

CAT ACA ATG CAG GTC TGT ACA ACC CAC CCT ACA GTG CTC AGT CAC ACC 255 His Thr Met Gln Val Cys Thr Thr His Pro Thr Val Leu Ser His Thr

CTG CTG CAA AGA CCC AAA CCT ACA GAC CCC AGG 288 Leu Leu Gln Arg Pro Lys Pro Thr Asp Pro Arg 10

#### (2) INFORMATION FOR SEQ ID NO: 160:

# (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 286 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Umbilical cord

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(117..284)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 40..207

id H54590

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 120..284

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 78..242

id AA143123

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (182..284)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 334..436

id AA142922

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(132..181)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 90

region 436..485

id AA142922

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 231..284

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 10..63

id AA013161

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 231..284

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 10..63

id AA018245

est

-5

AGA CCC ATG

Arg Pro Met

60

120

180

229

277

286

143	
(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 188244  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 6.1  seq IILLIHTMQVCTT/HP	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:	
AACTTCTCAT GAATGTTATG CTGTGTGGG CAGAGAAGA AAGCTGTTGA TGGGAGAGAA	Ĺ
TTACACAATC TGTTTTCCA TTTGAATGAA ACATCATGAA CATTGCGATT TTGTTAAATG	ì
ACAGTCGACC GGCCCAAGGA CTGGTACAAG ACGATGTTTA AGCAAATTCA CATGGTGCAC	:
AAGCCGG ATG ATG ACA CAG ACA TGT ATA ATA CTC CTT ATA CAT ACA ATG Met Met Thr Gln Thr Cys Ile Ile Leu Leu Ile His Thr Met	

CAG GTC TGT ACA ACC CAC CCT ACA GTG CTC AGT CAC ACC CTG CTA

Gln Val Cys Thr Thr His Pro Thr Val Leu Ser His Thr Leu Leu Gln

## (2) INFORMATION FOR SEQ ID NO: 161:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 355 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 176..321
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

region 158..303 id R59094

est

(ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 101..176
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 82..157

id R59094

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 56..104
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 38..86

id R59094 est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 177..256
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 193..272

id R35689

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 101..171
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 117..187

id R35689

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 60..104
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 77..121

id R35689

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 101..171
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 115..185

id H11787

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 39..104
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 54..119

id H11787

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 2..31
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 17..46

id H11787 est

,	i	٠,١	FEATURE:
1	1	х	PLAIURE:

- (A) MAME/KEY: sig\_peptide
- (B) LOCATION: 110..184
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6

seq LLGLLVAVATVHL/VI

55

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

60	CGGCTG	TAAC	STG (	GCA	AGT	STGG	ATGC	AC	rgcgo	AGC1	CG GC	CCCC	GACGO	AG	rtcgi	AGC
118	CT GGA la Gly	t Al		CTG	AAGO	TGA	SAAGO	GT(	GTAC	rgaa(	CT G	GGC	CTGT	GCA	CTC	GTGT
166													TCA Ser			
				-10					-15					-20		
214	Glu												GTC Val		Ala	
	10					5				1					-5	
262													CTG Leu			
310													TAC Tyr 30			
355													CCA			

## (2) INFORMATION FOR SEQ ID NO: 162:

45

# (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 401 base pairs

50

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 37..336
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98 region 18..317

id H73135 est

ł	i.	x	) F	EA	T	IJR	E	•

(A) NAME/KEY: other (B) LOCATION: 336..384

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 318..366

id H73135

est

### (ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 25..85

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 1..61 id AA251602

est

### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 30..95

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.9

seq LIYILWQLTGSAA/SG

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

ATTI	CAGT	GG C	TGAC	TTCC	A GA	GAGC	TAA			TCC Ser			53
	CTC Leu												101
	GTG Val								 		 	 	149
	AAG Lys 20						-				 	 	197
	ACC Thr		-					•			 	 	245
	CAA Gln												293
	CTG Leu												341
	GGG Gly												389

100

· insule of

85

GTG CTG CAT GTC Val Leu His Val

401

(2)	INFORMATION	FOR	SEO	ID	NO:	163:
-----	-------------	-----	-----	----	-----	------

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 241 base pairs

90

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 177..233
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 91 region 314..370 id T47889

est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 179..232
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.8 seq CFIILGLIICIQC/ST
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

AAAAGCCSSA CTTATTTTGG AAACTTGTAG CCAGAAAAAT TAGAATTTAA TTTAAGCAGT 60

AGAAAATAAT AAAAACTGAA AAATGTTAGG CAACACTAGA ATTTAACAAC AGGTGTGCTA 120

TGGTTTTTTA AATATAATTT TCTTTTTCCA GTTTCCCATT TTTATTAAAA GACAAATC 178

ATG GTA GGA ATG GTT TGC TTT ATT ATA CTT GGC TTA ATT ATT TGC ATA 226

Met Val Gly Met Val Cys Phe Ile Ile Leu Gly Leu Ile Ile Cys Ile

-15 -10 -5

CAG TGC AGC AGG GGG

Gln Cys Ser Thr Gly

1

## (2) INFORMATION FOR SEQ ID NO: 164:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 352 base pairs

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

## (ii) MOLECULE TYPE: CDNA

### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Umbilical cord

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (5..325)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 10..330

id W27422

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 22..250
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93

region 151..379

id AA153616

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 75..158
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 228..311

id R19252

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 24..75
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 178..229

id R19252

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 226..349
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 1..124

id W03861

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 24..123
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 139..238

### id AA029575 est

, :	1 12	FEATURE	
ľ	ı x	P P. ATTURE.	3

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 5..43
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.7

seq MXLLHSLSSGVRA/PS

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

ACAA			ı His			G13			A TCT Ser	49
					GLY GGG					97
					CCT Pro					145
					GCT Ala					193
					GGC Gly					241
					TGG Trp 75					289
					GAC Asp					337
CAA Gln										352

## (2) INFORMATION FOR SEQ ID NO: 165:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 356 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR

## (ii) MOLECULE TYPE: CDNA

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia

W - 5

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 16..347
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..332

id W56567

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 15..347
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 1..333

id AA151004

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 15..296
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 1..282

id AA147584

est ·

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 293..338
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 280..325

id AA147584

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 53..296
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 1..244

id W07033

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 293..337
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 242..286

id W07033

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 55..338
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94 region 1..284

id H94668

est

ı	ix	FEATURE:	
١.	40.		

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 285..341
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.6

seq PTLCVSSSPALWA/AS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

AACGCCTWTA	AGACAGCGGA ACTAAGAAAA	GAAGAGGCCT	GTGGACAGAA CAATCATGTC	60
TGACTCCCTG	GTGGTGTGCG AGGTAGACCC	AGAGCTAACA	GAAAAGCTGA KGAAATTCCG	120
CTTCCGAAAA	GAGACAGACA ATGCAGCCAT	CATAATGAAG	GTGGACAAAG ACCGGCAGAT	180
GGTGGTGCTG	GAGGAAGAAT TTCAGAACAT	TTCCCCAGAG	GVGCTCAAAA TGGAGTTGCC	240
GGAGAGACAG	CCCAGGTTCG TGGTTTACAG	CTACAAGTAC	GTGC ATG ACG ATG GCC Met Thr Met Ala	296
	ACC CTT TGT GTT TCA 1 Thr Leu Cys Val Ser 1 -10			344
AGC GAA ACA Ser Glu Thr				356

## (2) INFORMATION FOR SEQ ID NO: 166:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 463 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (li) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 182..352
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97 region 179..349 id AA057016

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 22..183
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

· -- -- ---

region 20..181 id AA057016 est

### (ix) FEATURE:

- (A) NAME/KEY: other(B) LOCATION: 22..183
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 23..184 id AA133917

est

## (ix) FEATURE:

- (A) NAME/KEY: other (B) LOCATION: 182..293
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 182..293

id AA133917

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 291..332
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 290..331

id AA133917

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 182..308
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 119..245

id R13065

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 80..183
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 18..121

id R13065

est

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 65..139
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.5

seq AQLFACLLRLGTQ/QV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

						13	3				
GAAC		: Va:			a Val			o Ar		G CTC	109
				AGG Arg -5							157
				AGC Ser							205
				AGT Ser							253
				GAG Glu							301
				ATC Ile 60							349
				CGT Arg							397
				AGA Arg							445
	Thr		GAC Asp					-			463

## (2) INFORMATION FOR SEQ ID NO: 167:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 370 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 34..282
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 29..277

id HUM413F04B

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 272..363
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 268..359 id HUM413F04B

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 27..181
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..155

id R13204

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 174..282
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 147..255

id R13204

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 275..344
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 249..318

id R13204

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 27..282
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 1..256

id R55599

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 275..344
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 250..319

id R55599

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 27..344
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97 region 1..318 id H23092

est

(ix)	FEATURE:
( X ( )	PEATURE:

(A) NAME/KEY: other

(B) LOCATION: 40..282

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 1..243 id C05240

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 272..363

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 234..325

id C05240

est

## (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 68..325

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.5

seq ALLTGPTLGSSQA/RW

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167:

AACG	AACG	CA C	GGCC	GCGC	CA SA	TCTG	TCTT	GC1	GGAA	CTT	TTTC	CTAC	GAG C	TTGA	GCGGT	60
TTGC	ACA			_	ATG Met									- , -		109
AGT Ser					GAT Asp											157
					GGG Gly											205
					CTC Leu -35											253
					SCG Xaa											301
					AGC Ser								_			349
		Thr			CCT Pro	-				٠.				•	٠	370

-

### (2) INFORMATION FOR SEQ ID NO: 168:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 354 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 51..195
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 38..182

id W38899

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 197..324
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 94

region 183..310

id W38899

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (207..349)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 141..283

id W93646

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (58..195)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 455..592

id W93646

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (3) LOCATION: 47..195
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95

region 32..180

id W19506

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 197..324

(C) IDENTIFICATION METHOD: blastn
(D) OTHER INFORMATION: identity 94

region 181..308

id W19506

est

## (ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 197..338

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 194..335

id W52820

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 71..195

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 69..193

id W52820

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 65..195

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 9..139

id W93906

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 207..269

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 309..371

id W93906

est

## (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 244..288

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.3

seq IVSVLALIPXTTT/LT

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

AGAGCTGTNN CNSAAGTAGG GGAGGGCGGT GCTCCGCMGM GGTGGCGGDH TGCTATCGCT 60

TCGCAGAACC TACTCAGGCA GCCAGCTGAG AAGAGTTGAG GGAAAGTGCT GCTGCTGGGT 120

CTGCARACGC GATGGATAAC GTGCAGCCGA AAATAWAACA TCGMCCCTTC TGCTTCAGTG 180

TGAAARGCCA CGTGAYRGAW DCTGCGGCTG GATATTATCA ACTCACTGGT AACAACAGTA 240

-

TTC ATG CTC ATC GTA TCT GTG TTG GCA CTG ATA CCA GAD ACC ACA ACA

Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Xaa Thr Thr Thr

-15

TTG ACM GTT GGT GGA GGG GTG TTT GCH HTT GTG ACA GCA GTA TGC TGT

Leu Thr Val Gly Gly Gly Val Phe Ala Xaa Val Thr Ala Val Cys Cys

1 5 10 15

CTT GCC GAC GGG GGG GGG

CTT GCC GAC GGG GGG GGG

354

Leu Ala Asp Gly Gly Gly

20

### (2) INFORMATION FOR SEQ ID NO: 169:

### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 245 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 55..242
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99 region 25..212

region 25..212 id AA022775

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 55..242
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 23..210

id R77353

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 55..242
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 16..203

id W17384

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 55..242
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

· Marinet of

region 19..206 id R05902 est

ı		FEATURE:	
1	ix)	PLATURE	

(A) NAME/KEY: other

(B) LOCATION: 55..242

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 16..203

id W76289

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 96..182

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5

seq ELSLLPSSLWVLA/TS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

AAGAGACGTC ACCGGCTGCG CCCTTCAGTA TCGCGGACGG AAGATGGCGT CCGCCACCCG 60

TCTCATCCAG CGGCTGCGGA ACTGGGCGTC CGGCC ATG ACC TGC AGG GGA AGC Met Thr Cys Arg Gly Ser -25

TGC AGC TAC GCT ACC AGG AGA TCT CCA AGC GAA CTC AGC CTC CTC CCA Cys Ser Tyr Ala Thr Arg Arg Ser Pro Ser Glu Leu Ser Leu Leu Pro -20 -15 -10

AGC TCC CTG TGG GTC CTA GCC ACA AGC TCT CCA ACA ATT ACT ATT GCA Ser Ser Leu Trp Val Leu Ala Thr Ser Ser Pro Thr Ile Thr Ile Ala -5 1 5

CTC GCG ATG GCC GCC GGG AAT CTG TGC CCC CTT AGG 245

Leu Ala Met Ala Ala Gly Asn Leu Cys Pro Leu Arg

### (2) INFORMATION FOR SEQ ID NO: 170:

10

### (i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 222 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

## (ii) MOLECULE TYPE: CDNA

## (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Umbilical cord

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 20..220

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 17..217

id W24468

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 102..220
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 75..193

id H71267

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 28..62
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 1..35

id H71267

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 68..97
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93

region 40..69

id H71267

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 45..220
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 3..178

id W38688

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 45..220
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 3..178

id W80906

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 52..220
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 1..169

id AA037518

est

## (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

5553 PCT/
(B) LOCATION: 4993 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.9 seq AVVFVFSLLDCCA/LI
SEQUENCE DESCRIPTION: SEQ ID NO: 170:
NGGTTTGACG GAAGGAGCGG CGGCGACGGA GGAGGAGG ATG GAG GCG Met Glu Ala -15

57 105 Val Val Phe Val Phe Ser Leu Leu Asp Cys Cys Ala Leu Ile Phe Leu -10 TCG GTC TAC TTC ATA ATT ACA TTG TCT RAT TTA GAA TGT GAT TAC ATT 153 Ser Val Tyr Phe Ile Ile Thr Leu Ser Xaa Leu Glu Cys Asp Tyr Ile 5 AAT GCT AGA TCA TGT TGC TCA AAA TTA AAC AAG TGG GTA ATT CCA GAA 201 -Asn Ala Arg Ser Cys Cys Ser Lys Leu Asn Lys Trp Val Ile Pro Glu 25 30 TTG ATT GGC CAT ACC ATT GGG 222 Leu Ile Gly His Thr Ile Gly 40

## (2) INFORMATION FOR SEQ ID NO: 171:

-

### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 249 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 14..197
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..184

id AA043611

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 193..251
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96 region 179..237

id AA043611

est

60

111

207

	WO 99/065	162 PC	PCT/I
	(ix)	FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 79168	
		(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.9 seq VAHALSLPAQSYG/ND	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 171:	
AGO	CCAGTWGA	GAAGGACTCT GATCCGGCTC AGCTTTCCAA TCAGCTGCGG AAGGAGCCA	C
GC	rttcgggg	GTTGCAAG ATG GCG GCC ACC AGT GGA ACT GAT GAG CCG GTT  Met Ala Ala Thr Ser Gly Thr Asp Glu Pro Val  -30 -25 -20	

TCC GGG GAG TTG GTG TCW GTG GCA CAT GCG CTT TCT CTC CCA GCA CAG Ser Gly Glu Leu Val Ser Val Ala His Ala Leu Ser Leu Pro Ala Gln

TCG TAT GGC AAC GAT CCT GAC ATT GAG ATG GCT TGG GCC ATG AGA GCA

Ser Tyr Gly Asn Asp Pro Asp Ile Glu Met Ala Trp Ala Met Arg Ala

1 5 10

ATG CAG CAT GCT GAA GTC TAT TAC AAG CTG ATT TCA TCA GTT (249)
Met Gln His Ala Glu Val Tyr Tyr Lys Leu Ile Ser Ser Val

-10

### (2) INFORMATION FOR SEQ ID NO: 172:

15

-15

------

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 406 base pairs

20

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 212..349
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

region 158..295

id W48792

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
    (B) LOCATION: 54..181
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 2..129 id W48792

est

(ix)	FEATURE:
------	----------

- (Λ) NΛME/KEY: other
- (B) LOCATION: 2..136
- ( ) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 15..149 id HOMO31HO1B

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 137..222
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 149..234

id HUMO31HO1B

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 207..248
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 220..261

id HUM031H01B

est

### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 275..325
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.6

seq ALFLLHNEMVSG/VY

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:

•	
AATCTCAGCT GGTTGGCTTT GGTTAGAGCT CCCGTCAGAC TTTCGTTCGG CCCTAGGATT	60
TGGTAGCCCC GAAGTGTGGG CTCTCTCCAG TACCAGACTC ATTTCAGTAC CAGCCTTTGG	120
GAAGTCGTGT GAATACCTCG GTCTCTTAGC CACAGGGATA GAATGGCGGC CTGACGGAGC	180
CGCGGCGCCG GCGAAGTCGC TGAGGCGCGA GCTGGAACCC CCAGACCAGC TCAAACGGGA	240
GCCAAAACTC GAAGCTTGGA AGAATTAGCA GGAA ATG GCG GAT GAG GCG TTG TTT  Met Ala Asp Glu Ala Leu Phe  -15	295
TTG CTT CTC CAT AAC GAG ATG GTG TCT GGA GTG TAC AAG TCC GCG GAS Leu Leu Leu His Asn Glu Met Val Ser Gly Val Tyr Lys Ser Ala Xaa -10 -5 1 5	343
ANG GGG AGG TGG ANA ACG GAC GAT GTA TTA CTA AGC TGG ANA ACA TGG	391

Xan Gly Arg Trp Lys Thr Asp Asp Val Leu Leu Ser Trp Lys Thr Trp

10 15 20

GGT TTC GAG TGG GAC Gly Phe Glu Trp Asp 406

### (2) INFORMATION FOR SEQ ID NO: 173:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 399 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymphocytes
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 16..307
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99

region 1..292

id H87111

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 92..352
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100

region 2..262

id W02272

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 173..400
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100

region 2..229

id W30926

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 68..198
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 92

region 20..150

id R57641

est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 22..378
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.3

seq SVCLSIISMLSSC/KE

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 173:

ACTTGGGGGG ATGGTTCCAT C ATG GCG TCA ATG CAG AAA CGA CTA CAG AAA Met Ala Ser Met Gln Lys Arg Leu Gln Lys -115 -110	51
GAA CTG TTG GCT TTG CAA AAT GAC CCA CCT CCT GGA ATG ACC TTA AAT Glu Leu Leu Ala Leu Gln Asn Asp Pro Pro Pro Gly Met Thr Leu Asn -105 -100 -95	99
GAG AAG AGT GTT CAA AAT TCA ATT ACA CAG TGG ATT GTA GAC ATG GAA Glu Lys Ser Val Gln Asn Ser Ile Thr Gln Trp Ile Val Asp Met Glu -90 -85 -80	147
GGT GCA CCA GGT ACC TTA TAT GAA GGG GAA AAA TTT CAA CTT CTA TTT Gly Ala Pro Gly Thr Leu Tyr Glu Gly Glu Lys Phe Gln Leu Leu Phe -75 -65	195
AAA TTT AGT AGT CGA TAT CCT TTT GAC TCT CCT CAG GTC ATG TTT ACT Lys Phe Ser Ser Arg Tyr Pro Phe Asp Ser Pro Gln Val Met Phe Thr -60 -55 -50	243
GGT GAA AAT ATT CCT GTT CAT CCT CAT GTT TAT AGC AAT GGT CAT ATC Gly Glu Asn Ile Pro Val His Pro His Val Tyr Ser Asn Gly His Ile -45 -35 -30	291
TGT TTA TCC ATT CTA ACA GAA GAC TGG TCC CCA GCG CTC TCA GTC CAA  Cys Leu Ser Ile Leu Thr Glu Asp Trp Ser Pro Ala Leu Ser Val Gln  -25  -20 -15	339
TCA GTT TGT CTT AGC ATT ATT AGC ATG CTT TCC AGC TGC AAG GAA AAG Ser Val Cys Leu Ser Ile Ile Ser Met Leu Ser Ser Cys Lys Glu Lys -10 -5 1	387
AGA CGA CCA CCG Arg Arg Pro Pro 5	399

## (2) INFORMATION FOR SEQ ID NO: 174:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 425 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 265..426
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96 region 57..218

· •

id AA083634 est

1	i v	٠١	FEATURE:	
ι	TX		FEATURE	

- (A) NAME/KEY: other
- (B) LOCATION: 262..420
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 91

region 63..221

id W71503 est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 265..420
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 91

region 193..348

id W55411

est

### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 249..329
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.1

seq VLMFCVTPPELET/KX

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:

AAGAACATCA GAAGTATATC TACATGAAGA ATTACAGCAA GACATGCAAA AGTTTAAGAA	60
TGAGGTCAAC ACATTAGAAG AAGAGTTCCT GGCTTTGAAG AAAGAAAATG TTCAACTTCA	120
TAAAGAGGTT GAAGAAGAAA TGGAGAAGCA CAGAAGTAAT AGCACAGAAT TATCAGGAAC	180
CCTAACTGAT GGTACTACTG TTGGCAATGA TGATGATGGA CTAAATCAGC AGATTCCTAG	240
GAAGGAAA ATG AAG ADM ATG ACA GGC TCT GAA AAT TGG AAA ACC AAG AAG Met Lys Xaa Met Thr Gly Ser Glu Asn Trp Lys Thr Lys Lys -25 -20 -15	290
GTT TTG ATG TTT TGT GTG ACG CCA CCT GAA TTA GAA ACC AAG RTG AAC Val Leu Met Phe Cys Val Thr Pro Pro Glu Leu Glu Thr Lys Xaa Asn -10 -5 1	338
ATA ACC AAA GGT GGT CTG GTG TTG TTT WCA GCA AAC TCG AAT TCA TCA Ile Thr Lys Gly Gly Leu Val Leu Phe Xaa Ala Asn Ser Asn Ser Ser 5 10 15	386
TGT ATG GAG CTA TCA AAG AAA ATT GCA GAG CGG CCA GCG Cys Met Glu Leu Ser Lys Lys Ile Ala Glu Arg Pro Ala 20 25 30	425

# (2) INFORMATION FOR SEQ ID NO: 175:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 176 base pairs

WO 99/06553		167	PCT/IB98/01
(c)	TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	167	
(ii) MOLE	CULE TYPE: CDNA		
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Lymphocyt		
(B) (C)	NAME/KEY: other LOCATION: 18170 IDENTIFICATION METHOD OTHER INFORMATION: ic	dentity 94 egion 45197 d AA102765	
(B) (C) (D)	NAME/KEY: sig_peptide LOCATION: 60158 IDENTIFICATION METHOD OTHER INFORMATION: se	: Von Heijne matrix core 4.1 eq LFMTRTLCSPGPS/Q	
AAGACGATTG GTCG	GGCCAC GCCAGATCTC AGGA	TGATGG GGCGCACCTG	GGGTTTGCC 59
	GTG GGT GTG CCC CAC G Val Gly Val Pro His V -25		
	CTC TTC ATG ACC AGG A Leu Phe Met Thr Arg T -10		
AGC CAG CCC AGA Ser Gln Pro Arc			176
(i) SEQUI	N FOR SEQ ID NO: 176: ENCE CHARACTERISTICS: LENGTH: 302 base pair TYPE: NUCLEIC ACID	·s -	

# (2) INFOR

- (i)
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other

(B) LOCATION: 33..229

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 2..198 id W87850

est

(ix) FEATURE:

\*

(A) NAME/KEY: other

(B) LOCATION: 209..298

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 179..268

id W87850

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 200..298

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 1..99

id AA043526

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 227..298

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 1..72

id H68037

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 235..298

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 3..66

id N78231

est

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 99..155

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 3.8

seq ALALASSQSHLLG/RD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 176:

AATTAAGTTC CGTTGTGGTT CACTCTGGTA TATCCTCTGA AAGTGGGCAT TACTATTCTT

ATGCCAGAAA TATCACAAGT ACAGACTCTT CATATCAG ATG TAC CAC CAG TCT GAG 116

Met Tyr His Gln Ser Glu

-15

GCT CTG GCA TTA GCA TCC TCC CAG AGT CAT TTA CTA GGG AGA GAT AGT
Ala Leu Ala Leu Ala Ser Ser Gln Ser His Leu Leu Gly Arg Asp Ser

---

-10

### (2) INFORMATION FOR SEQ ID NO: 177:

### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 213 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Umbilical cord

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(61..133)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98 region 46..118 id R15459 est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (142..180)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 1..39 id R15459 est

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 52..117
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.8

seq FASVAMICAIASG/SE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 177:

WO 99/06553 PCT/IB98/01237 170

		GCA Ala						105
		TCG Ser 1						.153
		GTT Val						201
 CGC Arg 30	-						42	213

### (2) INFORMATION FOR SEQ ID NO: 178:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 264 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (15..226)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 1..212 id N56211

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 125..198
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 87..160 \_ id W37072

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 72..127
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 35..90

id W37072

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 191..245

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 92

region 152..206

id W37072

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 38..73

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 2..37

id W37072

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 125..249

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 87..211

id W37073

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 72..124

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 35..87

id W37073

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 38..73

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 2..37

id W37073

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 52..235

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 1..184

id T84830

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 52..127

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 1..76

id AA069888

est

(ix)	FEAT	URE:						
	(A)	NAME/I	KEY:	othe	r			
	(B)	LOCAT	ION:	125.	.198			
	(C)	IDENT:	FIC	ATION	METH	DD:	blastn	
	(D)	OTHER	INF	ORMAT	ION:	req id	entity 9 gion 73. AA06988	.146
						est	Ē.	
	EE A T	mr.						

## (ix) FEATURE:

- (A) NAME/KEY: other (B) LOCATION: 191..243
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94 region 138..190 id AA069888

est

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 115..204
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.7

seq SMMLLTVYGGYLC/SV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 178:

ACGA	GTG	CTG (	CGTTC	CGGC	rg To	SCTGO	GAAG	TTC	GCGT?	AGAC	AGTO	GCC1	rcg 1	AGAC	CCTGCC	60
TGCC	TGAC	GGA (	GCC1	rcgg	TT GO	SATGO	CGAAC	GA(	CTG	CAGC	ATC	CAGGO	GA (	CAAG	ATG Met -30	117
							GAC Asp								Thr	165
							TAT Tyr									213
							CGC Arg									261
GGG Gly 20					J.			٠.								264

### (2) INFORMATION FOR SEQ ID NO: 179:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 97 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA

ĺ	'vi '	ORIGI	NAT.	SOUR	CF.
۱	· v	CIVEGE	עמוו.	3000	، ندا

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (2..95)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 231..324

id N32226

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (2..85)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 243..326

id N32240

est

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 44..85
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.5

seq FPVCLTVTAAVCG/XX

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 179:

AACACATTTC TGTATCGCCC CGTGAAGAGC TCTACGCACA TGA ATG TTC CCC GTC 55

Met Phe Pro Val

TGT TTA ACT GTT ACG GCM GCA GTG TGT GGG CNG CAS GCA CAG
Cys Leu Thr Val Thr Ala Ala Val Cys Gly Xaa Xaa Ala Gln
-10 -5 1

97

## (2) INFORMATION FOR SEQ ID NO: 180:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 241 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR

### (ii) MOLECULE TYPE: CDNA

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 60..240
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

\*\*\*

region 66..246 id R89543 est

1		i	x	١	F	F	Δ	T	11	D	E	
ı	ι.	L	л	3	Г	C.	•		u	п	·Ľ	-

- (A) NAME/KEY: other
- (B) LOCATION: 60..223
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 66..229

id H59647

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 49..205
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 34..190

id N34164

est

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 95..139
- (C): IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.5

seq VIFFACVVRVRDG/LP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 180:

## AAAGATTGCT GAGGAGGCGG CGGGTAGCTG GCAGGCGCCG ACTTCCGAAN GCCGCCGTCC 60

GGGCGAGGTG TCCTCATGAC TTCTCTTGTG GACC ATG TCC GTG ATC TTT TTT GCC 115

Met Ser Val Ile Phe Phe Ala

-15
-10

TGT GTG GTA CGG GTA AGG GAT GGA CTG CCC CTC TCA GCC TCT ACT GAT

Cys Val Val Arg Val Arg Asp Gly Leu Pro Leu Ser Ala Ser Thr Asp

TTT TAC CAC CAA GAT TTT TTG GAA TGG AGG AGA CGG CTC AAG AGT
Phe Tyr His Thr Gln Asp Phe Leu Glu Trp Arg Arg Arg Leu Lys Ser

TTA GCC TTG CGA CTG GCC CAG TAT CCA GGG
Leu Ala Leu Arg Leu Ala Gln Tyr Pro Gly
25
30

### (2) INFORMATION FOR SEQ ID NO: 181:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 316 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA

.:

### (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens(F) TISSUE TYPE: Lymphocytes

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 80..256

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 68..244

id H46779

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 249..312

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 238..301

id H46779

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 80..312

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 68..300

id H46081

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 73..293

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 2..222

id W07846

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 262..312

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 192..242

id W07846

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 80..283

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 12..215

id AA022743

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 27	8	312
------------------	---	-----

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 256..290 id AA022743

est

### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 50..253

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 3.5

seq LVLDVVMLLLYLG/IE

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 181:

ACCCTGTTTC CGGCAGCGCS CGCTGCTCCG GGAGCCGCTG TGGCAGCGT ATG CTS AVG Met Leu Xaa									
		AAA CGG TTG TCC TCC ACC CCG Lys Arg Leu Ser Ser Thr Pro -55 -50	.06						
	he Phe Leu Asn Gly	TGG TAT AAT GCT ACC TAT TTC Trp Tyr Asn Ala Thr Tyr Phe -40 -35	.54						
		AAA GGT GTC CTG CTA CCA TAT Lys Gly Val Leu Leu Pro Tyr -20	202						
		GTG ATG CTC CTC CTT TAT CTT 2 Val Met Leu Leu Leu Tyr Leu -5	50						
		GGT ACA AAG GGA AAC CTC TGC 2 Gly Thr Lys Gly Asn Leu Cys 10 15	98						
CAG CGA AAG ATG CO		3	16						

## (2) INFORMATION FOR SEQ ID NO: 182:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 292 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

## (ii) MOLECULE TYPE: CDNA

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- ·(F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:

	(B) LC	AME/KEY: ( OCATION: ( DENTIFICA: THER INFO	complem CION ME	THOD: b l: ider regi	last:	n 97 3245			•	
(ix)	FEATURE	E:						•		
•		AME/KEY: (			20	٥,				
		CATION: ( DENTIFICAT	-							
		THER INFO			tity					
				-	on 6: 10581	5241 0	,	-:		
				esc						
(ix)	FEATURE						•			•
		AME/KEY: ( CATION: (		.aat /131	20	٥,				
		DENTIFICA:	_			-				
		THER INFO		l: ider	tity	98				
				_		7195				
				est	ISC20	E U 4 Z			: i	
(ix)	FEATURE	Ε:								
		AME/KEY:							•	
		CATION: 2 DENTIFICAT			last	n				
		THER INFO		N: ider regi	tity on 1	100 45				
(ix)	FEATUR	E:								
,		AME/KEY:								
		OCATION: ! DENTIFICA!			lon U	aiina m	atriv			
_		THER INFO		N: sco	re 3.	_				
(xi)	SEQUEN	CE DESCRI	PTION:	SEQ ID	NO:	182:				
AACTCTCTGG	CCTGTG	TCTA GTTG	TTTGAT	TCAGAC	AGCT	GCCTGG	GATC C	CTCATC	CTC	60
ATACCCACCC	CCACCC	AAGG GCCT	GGCCTG	AGCTGG		ATT GO : Ile GI -35				115
TGG GAT CC Trp Asp Pr -30									g	163
AGG CCA GC Arg Pro Al	a Leu T				Gly					211

TCC CAA CTC ACC CCA GCC CCA AAA CTC TCC TCT GCT GCT GGC TGG TTA Ser Gln Leu Thr Pro Ala Pro Lys Leu Ser Ser Ala Ala Gly Trp Leu

1237

209

257

266

WO 99/06553		178	PCT/IB98/0
5	10	15	
	GAC GCC ATC CCA GCC Asp Ala Ile Pro Ala 25		292
			• •
(2) INFORMATION	FOR SEQ ID NO: 183:		
(A) (B) (C)	NCE CHARACTERISTICS: LENGTH: 266 base pa TYPE: NUCLEIC ACID STRANDEDNESS: DOUBL TOPOLOGY: LINEAR		
(ii) MOLE	CULE TYPE: CDNA	·.	
(A)	INAL SOURCE: ORGANISM: Homo Sapi TISSUE TYPE: Lymph		
(B) (C)	NAME/KEY: other LOCATION: 96252 IDENTIFICATION METH	OD: fasta identity 98 region 1157 id HSU41901 vrt	· : : : : : : : : : : : : : : : : : : :
(B) (C)	URE: NAME/KEY: sig_pepti LOCATION: 96179 IDENTIFICATION METH OTHER INFORMATION:	OD: Von Heijne mat:	
(xi) SEQU	ENCE DESCRIPTION: SE	Q ID NO: 183:	
AGTGGATSMW AGNN	CCGTGT TGGTGAAGCC TO	TCCTCGCG AGCAGCGCG	C ACCCCTCCAG 60
AGCACCCCGC GGAC	CCGCAC CTCGGCGTGG CC	ACC ATG GTC AGG AG Met Val Arg Ar -2	g Val Gln
	CAG TTG CCA CTG GTC Gln Leu Pro Leu Val -15		

CTT CCC ACA GGA CTG CCT GTT CGC AGC GTG GAT TTT AAC CGA GGC ACG

Leu Pro Thr Gly Leu Pro Val Arg Ser Val Asp Phe Asn Arg Gly Thr

GAC AAC ATC ACC GTG AGG CAG GGG GAC ACA GCC ATC CTC AGA TTT CTC

Asp Asn Ile Thr Val Arg Gln Gly Asp Thr Ala Ile Leu Arg Phe Leu

15

VNC TCA GGG

Xaa Ser Gly

20

(2) INFORMATION FOR SEQ ID NO:	(2)	INFORMATION	FOR	ろむひ	ΤD	NO:	T94:
--------------------------------	-----	-------------	-----	-----	----	-----	------

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 332 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 52..327
  - (C) IDENTIFICATION METHOD: fasta
  - (D) OTHER INFORMATION: identity 97

region 4..280 id HUMGPCRB

vrt

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 293..327
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 94

region 1..35 id T29782

est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 180..236
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.4

seq LVFIIGLVGNLLA/LV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 184:

AACTTC	NNN HTG	GACAACT I	ACTCACAGC	r actaca	CWRA	GACCCGA	ATM GAG	rcactga	60
TATACA	CTG GAC	CACCACC I	\ATGGATAT	A CAAATG	GCAA	ACAATTT	TAC TCC	GCCTCTG	120
CAACTC	CTCA GGG	AAATGAC '	rgtgacctc	r atgcac	ATCA	CAGCACGO	GCC AGG	ATAGTA	179
			C CTC GTC c Leu Val						227
			C ATT GTT l lle Val 5						275
			A AAT TTG r Asn Leu						323

WO 99/06553 PCT/IB98/01237

15

20

25

ACC GTC GGG Thr Val Gly

332

### (2) INFORMATION FOR SEQ ID NO: 185:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 273 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 54..272
  - (C) IDENTIFICATION METHOD: fasta
  - (D) OTHER INFORMATION: identity 97

region 291..509

id D82060

vrt

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 82..243
    - (C) IDENTIFICATION METHOD: fasta
    - (D) OTHER INFORMATION: identity 98

region 1..162

id HUMMHCRING

vrt

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 61..150
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.5

seq WATLGLLVAGLGG/HD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 185:

AAAAG	GCGGG 1	ACTGO	CAC	ST CC	CAAGO	CAAAC	CGC	GAA	AGGA	GAG	SATCO	CCG	GAGCO	CGCGTG	60
	CC AGA la Arg														108
	GG GCG rp Ala														156
GAC C	TG CAC	GAC	GAT	CTG	CAA	GAG	GAC	TTC	САТ	GGC	CAC	AGC	רשר	AGG	204

181

Asp Leu His Asp Asp Leu Gln Glu Asp Phe His Gly His Ser His Arg
5 10 15

CAC TCA CAT GAA GAT TTC CAC CAT GGC CAM AGC CAT GGC CAT GGC CAT
His Ser His Glu Asp Phe His His Gly Xaa Ser His Ala His Gly His
20
25
30

GGC CAC AMT CAC GAG AGC ATG Gly His Xaa His Glu Ser Met 35 40

273

### (2) INFORMATION FOR SEQ ID NO: 186:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 32 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -14..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 11.8

seq VLVALILLHSALA/QS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 186:

Met Val Leu Val Ala Leu Ile Leu Leu His Ser Ala Leu Ala Gln Ser
-10 -5 1

Arg Arg Asp Phe Ala Pro Pro Gly Gln Gln Lys Arg Glu Ala Pro Gly 5 10 15

## (2) INFORMATION FOR SEQ ID NO: 187:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 68 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (3) LOCATION: -21..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix

- (D) OTHER INFORMATION: score 10 seq LLLCLQTWPEAAG/KD
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 187:
- Met Ala Gln His His Leu Trp Ile Leu Leu Cys Leu Gln Thr Trp
- Pro Glu Ala Ala Gly Lys Asp Ser Glu Ile Phe Thr Val Asn Gly Ile
  -5 1 5
- Leu Gly Glu Ser Val Thr Phe Pro Val Asn Ile Gln Glu Pro Arg Gln
  15 20 25
- Val Lys Ile Ile Ala Trp Thr Ser Lys Thr Ser Val Ala Tyr Val Thr 30 35 40

Pro Gly Glu Arg
45

- (2) INFORMATION FOR SEQ ID NO: 188:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 103 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (3) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 10

seq FLLLVTAPRCILS/QV

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 188:
- Met Lys Asp Leu Trp Ile Phe Leu Leu Leu Val Thr Ala Pro Arg Cys
  -15
  -10
  -5
- I'e Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Arg Leu Val Arg
- Pro Ser Glu Thr Val Ser Leu Ser Cys Thr Val Ser Gly Asp Ser Val
  15 20 25
- Ser Ser Gly Asp His Tyr Trp Thr Trp Leu Arg Gln Pro Pro Gly Gly 30 45
- Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Thr Thr Gly Lys Ile Asp Tyr
  50 55 60

-

Asn Pro Ser Xaa Arg Arg Arg Val Thr Ile Ser Val Asp Thr Ser Lys
65 70 75

Asn Leu Phe Ser Leu Thr Arg

- (2) INFORMATION FOR SEQ ID NO: 189:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 79 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Placenta
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 10 seq LLLCLQTWPEAAG/KD
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 189:
- Met Ala Gln His His Leu Trp Ile Leu Leu Cys Leu Gln Thr Trp
  -20 -15 -10
- Pro Glu Ala Ala Gly Lys Asp Ser Glu Ile Phe Thr Val Asn Gly Ile
  -5 1 5 10
- Leu Gly Glu Ser Val Thr Phe Pro Val Asn Ile Gln Glu Pro Arg Gln
  15 20 25
- Val Lys Ile Ile Ala Trp Thr Ser Lys Thr Ser Val Ala Tyr Val Thr 30 35 40
- Pro Gly Asp Ser Glu Thr Ala Pro Val Val Thr Val Thr His Met
  45 50 55
- (2) INFORMATION FOR SEQ ID NO: 190:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 58 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia

-

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -19..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9.9 seq FLFVVAAATGVOS/QV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 190:

Met Asp Trp Thr Trp Arg Phe Leu Phe Val Val Ala Ala Ala Thr Gly
-15 -10 -5

Val Gln Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
1 5 10

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Thr Ser Gly Asp Gly Phe
15 20 25

Ser Lys Tyr Pro Ile Asn Trp Val Gln Gly 30

- (2) INFORMATION FOR SEQ ID NO: 191:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 62 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 9.6 seq GLLLLCLLPHRLA/LV
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 191:

Met Ser Ile Cys Phe Leu Gly Leu Leu Leu Cys Leu Leu Pro His

Arg Leu Ala Leu Val Gln Lys His Ser Ser Pro Ser Ser Arg Leu Leu
1 5 10

Leu Ile Pro Val Val Gln Cys Leu Leu Ala Leu Glu Phe Leu Gln Asp 15 20 25

Pro Tyr Leu Asp Ile Phe Asn Leu Pro Leu Pro Pro Pro Trp 30 35 40

- 144-25-74-

#### (2) INFORMATION FOR SEQ ID NO: 192:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 22 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -17..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9.2

seq LVLLILPLLSSLS/KV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 192:

Met Ile Gly Phe Leu Val Leu Leu Ile Leu Pro Leu Leu Ser Ser Leu
-15 -10 -5

Ser Lys Val Ser Ser Lys 1 5

- (2) INFORMATION FOR SEQ ID NO: 193:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 39 amino acids
    - (3) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -31..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.9

seq LLMSLLVSTVTWQ/IS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 193:

Met Gln Cys Leu Leu Ser Val Leu Met Ala Gln Phe Ile Xaa His Phe
-30 -25 -20

Leu Ser Leu Leu Met Ser Leu Leu Val Ser Thr Val Thr Trp Gln Ile
-15 -5 1

Ser Arg Thr Pro Trp His Gly

THE TANK

5

### (2) INFORMATION FOR SEQ ID NO: 194:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 87 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -19..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.9 seq WIFFLATLKGVQC/QV
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 194:
- Met Glu Leu Gly Leu Ser Trp Ile Phe Phe Leu Ala Thr Leu Lys Gly
  -15 -10 -5
- Val Gln Cys Gln Val Arg Leu Leu Glu Ser Ala Gly Gly Leu Gln Glu
  1 5 10
- Pro Gly Gly Ala Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ile Phe 15 20 25
- Asn Asp Phe Ala Met His Trp Val Arg Gln Thr Pro Gly Lys Gly Leu 30 45
- Glu Trp Val Ala Gly Ile Asn Trp Asp Gly Xaa Ile Leu Gly Tyr Ala 50 55 60

Asp Ser Val Lys Gly Arg Arg 65

- (2) INFORMATION FOR SEQ ID NO: 195:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 59 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE: .
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:

-

- (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -15..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.6

seq SVSLALLSGWVGS/RQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 195:

Met Val Ser Val Ser Leu Ala Leu Leu Ser Gly Trp Val Gly Ser Arg

Gln Gly Arg Val Gly Leu Ser Thr Leu Val Thr Leu Gly Leu Val Ser 5 10 15

Trp Cys Trp Arg Met Val Arg Thr Gln Ala Leu Glu Gly Phe Leu Ser 20 25 30

Val Lys Tyr Tyr Ser Ala Phe Ser Ala Asp Gln
35 40

- (2) INFORMATION FOR SEQ ID NO: 196:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 57 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Placenta
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.5 seq LPLLLSWVAGGFG/NA
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 196:

Met Pro Leu Pro Trp Ser Leu Ala Leu Pro Leu Leu Ser Trp Val -20 -15 -10

Ala Gly Gly Phe Gly Asn Ala Ala Ser Ala Arg His His Gly Leu Leu -5 1 10

Ala Ser Ala Arg Gln Pro Gly Val Cys His Tyr Gly Thr Lys Leu Ala

Cys Cys Tyr Gly Trp Arg Arg Asn Ser 30 35

(2) INFORMATION FOR SEQ ID NO: 197:

\*\*\* E ---

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 114 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -80..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.4 seq FVVFSLFLICAMA/GD
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197:

Met Val Ser Asn Phe Phe His Val Ile Gln Val Phe Glu Lys Ser Ala
-80 -75 -70 -65

Thr Leu Ile Ser Lys Thr Glu His Ile Gly Phe Val Ile Tyr Ser Trp
-60 -55 -50

Xaa Lys Ser Thr Thr His Leu Gly Ser Arg Arg Lys Phe Ala Ile Ser
-45 -40 -35

Ile Tyr Leu Ser Glu Val Ser Leu Gln Lys Tyr Asp Cys Pro Phe Ser
-30 -25 -20

Gly Thr Ser Phe Val Val Phe Ser Leu Phe Leu Ile Cys Ala Met Ala
-15 -10 -5

Gly Asp Val Val Tyr Ala Asp Ile Lys Thr Val Arg Thr Ser Pro Leu
1 5 10 15

Glu Leu Ala Xaa Xaa Leu Gln Arg Ser Xaa Xaa Phe Asn Phe Ser Xaa -- 20 25 30

Xaa Arg

- (2) INFORMATION FOR SEQ ID NO: 198:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 80 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE: .
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:

and the Tame

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: -44..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 8.2

seq ICLACVLFPLLRT/SD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198:

Met Arg Xaa Phe Trp Phe Leu Met Tyr Pro Phe Arg Phe His Asp Cys
-40 -35 -30

Lys Gln Lys Tyr Asp Leu Tyr Ile Ser Ile Ala Gly Trp Leu Ile Ile
-25 -20 -15

Cys Leu Ala Cys Val Leu Phe Pro Leu Leu Arg Thr Ser Asp Asp Thr
-10 -5 1

Pro Gly Asn Arg Thr Lys Cys Phe Val Asp Leu Pro Thr Arg Asn Val 5 10 15 20

Asn Leu Ala Gln Ser Val Val Met Met Thr Ile Gly Glu Leu Ile Gly 25 30 35

# (2) INFORMATION FOR SEQ ID NO: 199:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 64 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -17..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7

seq CCLFTCFFIPCIS/CK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 199:

Met Val Ser Leu Cys Cys Leu Phe Thr Cys Phe Phe Ile Pro Cys Ile
-15 -10 -5

Ser Cys Lys Leu Glu Met Trp Gly Leu Asp Glu Pro Lys Val Lys Pro
1 5 10 15

Phe Trp Gln Glu Cys Val Leu Gly Asp Val Val Gly Xaa Ile Leu Gln 20 25 30

His Arg Arg Gln Pro Pro Val Pro Arg Ser Ile Leu Val Met Gly Ala 35 40 45 

#### (2) INFORMATION FOR SEQ ID NO: 200:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 30 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Placenta
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -27..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.9

seq ILLLVTYSPIAYS/HS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 200:

Met Asp Phe Phe Phe Leu Glu Arg Ser Tyr Trp Gly Lys Met Ile Leu -25 -20 -15

Leu Leu Val Thr Tyr Ser Pro Ile Ala Tyr Ser His Ser Arg
-10 -5 1

- (2) INFORMATION FOR SEQ ID NO: 201:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 55 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -26..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.9

seq LWVLLLCAHVVTL/LV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 201:

Met Thr Met Arg His Asn Trp Thr Pro Asp Leu Ser Pro Leu Trp Val
-25 -20 -15

Leu Leu Cys Ala His Val Val Thr Leu Leu Val Arg Ala Thr Pro

Val Ser Gln Thr Xaa Thr Ala Ala Thr Ala Ser Val Arg Ser Thr Lys

10 15 20

Asp Pro Cys Pro Thr Gln Gly
25

- (2) INFORMATION FOR SEQ ID NO: 202:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 59 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -48..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.8

seq ILRMLLSLQPVLQ/DA

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 202:
- Met Asp Asn Met Ser Gly Gly Lys Val Asp Glu Ala Leu Val Lys Ser
  -45 -40 -35
- Ser Cys Leu His Pro Trp Ser Lys Arg Asn Asp Val Ser Met Gln Cys
  -30 -25 -20
- Ser Gln Asp Ile Leu Arg Met Leu Leu Ser Leu Gln Pro Val Leu Gln
  -15 -10 -5
- Asp Ala Ile Gln Lys Lys Arg Thr Val Arg Gln
  1 5 10
- (2) INFORMATION FOR SEQ ID NO: 203:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 59 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide

- -

- (B) LOCATION: -45..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.7 seq AALVLWTLPGAOR/RG
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 203:

Met Xaa Leu Gln Gly Gln Glu Ala Thr Gly Lys Val Leu Ile Lys Ile
-45 -40 -35 -30

His Lys Asp Thr Ser Gln Val Pro Thr Ala Xaa Gly Asp Ala Ser Ile
-25 -20 -15

Ala Ala Leu Val Leu Trp Thr Leu Pro Gly Ala Gln Arg Arg Gly Glu
-10 -5 1

Phe Ala Pro Lys Gly Ala Pro Met Thr Asn Arg
5 10

- (2) INFORMATION FOR SEQ ID NO: 204:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 29 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -25..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.6 seq ILVLILFPTSCVM/QV
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 204:

Met Thr Glu His Ser Leu Thr His Gln Gly IIe Pro IIe Leu Val Leu -25 -15 -10

Ile Leu Phe Pro Thr Ser Cys Val Met Gln Val Leu Trp

- (2) INFORMATION FOR SEQ ID NO: 205:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 32 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

\*\*\*\*\*\*\*\*\*\*\*\*

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -19..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.5

seq RFIFLTSLQLISS/SY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 205:

Met Tyr Ile Gly Gly Leu Arg Phe Ile Phe Leu Thr Ser Leu Gln Leu
-15 -10 -5

Ile Ser Ser Ser Tyr Val Thr Thr Leu Leu Lys Lys Asn Thr Leu Arg

- (2) INFORMATION FOR SEQ ID NO: 206:
  - (i) SEQUENCE CHARACTERISTICS: (
    - (A) LENGTH: 41 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -38..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.5

seq LIFFSLIFLNLFA/IS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 206:

Met Ser Val Ser Leu Lys His Ile His Leu His Phe Ile Ile Met Ser
-35 -30 -25

Val Leu Val Phe Trp Asn Cys Ser His Leu Ile Phe Phe Ser Leu Ile
-20
-15
-10

Phe Leu Asn Leu Phe Ala Ile Ser Trp

- (2) INFORMATION FOR SEQ ID NO: 207:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 27 amino acids

-

- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -22..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.3

seq MVSFLSXPFLCSA/KP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:

Met Xaa Xaa Leu Gly Xaa Xaa Arg Phe Met Val Ser Phe Leu Ser Xaa -20 -15 -10

Pro Phe Leu Cys Ser Ala Lys Pro Ser Ser Gly
-5 1 5

- (2) INFORMATION FOR SEQ ID NO: 208:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 71 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.3

seq ILVSVAAATGAHS/QL

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 208:
- Met Asp Trp Trr Trp Tyr Ile Leu Val Ser Val Ala Ala Ala Thr Gly
  -15 -10 -5
- Ala His Ser Gln Leu Gln Leu Gln Ser Gly Ser Asp Ile Lys Lys
- Pro Gly Ala Ser Met Asn Val Ser Cys Lys Ala Ser Gly Gly Ser Ile 15 20 25
- Ser Thr Arg Gly Ile Ser Trp Val Arg Gln Val Pro Gly Gln Gly Leu 30 35 40 45

The Barrier

Glu Trp Met Gly Trp Ile Gly 50

- (2) INFORMATION FOR SEQ ID NO: 209:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 56 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -45..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.3

seq VACVLSSLIAVNS/AH

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 209:

Met Ile Ser Lys Phe Ser Ser Lys Ala Tyr Ser Val Arg Gly Leu Glu
-45 -35 -30

Leu Phe Ser Leu Leu Pro Ile Asn Pro Ser Pro Asn Ser Ala Ile Xaa
-25
-20
-15

Val Ala Cys Val Leu Ser Ser Leu Ile Ala Val Asn Ser Ala His Pro
-10 -5 1

Glu Ser Thr Ile Asp Thr Arg Trp
5 10

- (2) INFORMATION FOR SEQ ID NO: 210:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 30 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -28..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.3

### seq LLFLIFSLNLNRG/VG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 210:

Met Val Leu Gly Ala Phe Gly Ser Cys Ile Lys Ser Phe Ser Leu
-25 -20 -15

Leu Phe Leu Ile Phe Ser Leu Asn Leu Asn Arg Gly Val Gly
-10 -5 1

# (2) INFORMATION FOR SEQ ID NO: 211:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 105 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -35..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.3 seq ALKLLLSPGXSGS/SS
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 211:

Met Ala Ala Arg Gln Ala Val Gly Ser Gly Ala Gln Glu Thr Cys Gly
-35 -25 -25

Leu Asp Arg Ile Leu Glu Ala Leu Lys Leu Leu Ser Pro Gly Xaa
-15
-10
-5

Ser Gly Ser Ser Leu Gln Val Thr Lys His Asp Val Leu Leu Ala 1 5 10

Thr Leu Lys Ser Asn Leu Ser Ala Leu Glu Asp Lys Phe Leu Lys Asp
15 20 25

Pro Gln Trp Lys Asn Leu Lys Leu Leu Arg Asp Glu Ile Ala Asp Lys 30 35 40 45

Ala Glu Trp Pro Gln Asn Ser Val Asp Val Thr Trp Ser Phe Thr Ser 50 55 60

Gln Thr Leu Leu Leu Leu Cys Leu
65 70

(2) INFORMATION FOR SEQ ID NO: 212:

· •

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 55 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -19..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.2 seq LALFLMALGFSCI/HK
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 212:

Met Ser Thr Gln Lys Gly Leu Ala Leu Phe Leu Met Ala Leu Gly Phe
-15 -10 -5

Ser Cys Ile His Lys Lys Phe Gln Glu Ser Glu Glu Gly Lys His His

1 5 10

Met Gly Gly Ile Asn Arg Ser His Trp Val Lys Ser Arg Lys Ser Cys 15 20 25

Leu Ile Asn Ser Gln Arg Lys 30 35

- (2) INFORMATION FOR SEQ ID NO: 213:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 27 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -25..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.1

seq YFLIVFFVFLCNC/HQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 213:

Met Lys Asp Val Glu Ile Ile Met Ile Phe His Gly Tyr Phe Leu Ile -25 -15 -10

\*\*\* The

Val Phe Phe Val Phe Leu Cys Asn Cys His Gln -5

- (2) INFORMATION FOR SEQ ID NO: 214:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 44 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide -
    - (B) LOCATION: -42..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.1 seq AILLLQSQCAYWA/LP
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 214:
- Met Cys Phe Pro Glu His Arg Arg Gln Met Tyr Ile Gln Asp Arg Leu
  -40 -35 -30
- Asp Ser Val Thr Arg Arg Ala Arg Gln Gly Arg Ile Cys Ala Ile Leu
  -25 -20 -15

Leu Leu Gln Ser Gln Cys Ala Tyr Trp Ala Leu Pro
-10 -5 1

- (2) INFORMATION FOR SEQ ID NO: 215:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 33 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -23..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.1

seq SSILSTFVSWLSA/FY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 215:

Met Leu Val Val Lys Gln Cys Phe Ser Asp Ser Ser Ile Leu Ser Thr
-20 -15 -10

Phe Val Ser Trp Leu Ser Ala Phe Tyr Cys Lys Glu Gly Pro Ser Ser -5

Gly 10

### (2) INFORMATION FOR SEQ ID NO: 216:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 104 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -32..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.1

seq LPLLTSALHGLQQ/QH

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 216:
- Met Ile Xaa Leu Arg Asp Thr Ala Ala Ser Leu Arg Leu Glu Arg Asp
  -30 -25 -20
- Thr Arg Gln Leu Pro Leu Leu Thr Ser Ala Leu His Gly Leu Gln Gln
  -15 -5
- Gln His Pro Ala Phe Ser Gly Val Ala Arg Leu Ala Lys Arg Trp Val 1 5 10 15
- Arg Ala Gln Leu Leu Gly Glu Gly Phe Ala Asp Glu Ser Leu Asp Leu
  20 25 30
- Val Ala Ala Leu Phe Leu His Pro Glu Pro Phe Thr Pro Pro Ser 35 40 45
- Ser Pro Gln Val Gly Phe Leu Arg Phe Leu Phe Leu Val Ser Thr Phe 50 55 60
- Asp Trp Lys Asn Asn Pro Leu Gly 65 70
- (2) INFORMATION FOR SEQ ID NO: 217:
  - (i) SEQUENCE CHARACTERISTICS:

---

- (A) LENGTH: 17 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -14..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.9

seq ITMMLALISVCLF/AF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 217:

Met Ile Thr Met Met Leu Ala Leu Ile Ser Val Cys Leu Phe Ala Phe

Trp

- (2) INFORMATION FOR SEQ ID NO: 218:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 52 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.9

seq LLTLVQCSDLCPS/CS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 218:

Met Trp Leu Leu Thr Leu Val Gln Cys Ser Asp Leu Cys Pro Ser Cys
-15 -5 1

Ser Gln Ala Leu Thr Leu Val Leu Val Ser Phe Ser Glu Val Arg Asp
5 10 15

Leu Ala Glu Thr Ser Leu Ser Ser Asn Leu Lys Asn Ser Leu Phe Ile 20 25 30

Val Leu Lys Arg

# (2) INFORMATION FOR SEQ ID NO: 219:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 51 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -31..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.9 seq LLFACLTMLLVKT/CQ
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 219:

Met Arg Val His Leu Phe Pro Tyr Leu Cys Gln Pro Ser Val Leu Ser
-30 -25 -20

Asn Phe Leu Leu Phe Ala Cys Leu Thr Met Leu Leu Val Lys Thr Cys
-15
-5
1

Gln Glu Ser Pro Lys Ser Pro Leu Ser Leu Met Ile Cys Gln Thr Tyr
5 10 15

Arg Ile Gly

- (2) INFORMATION FOR SEQ ID NO: 220:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 47 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.7 seq PLCFLILPYPVLS/SH
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 220:

Met Ile Pro Leu Cys Phe Leu Ile Leu Pro Tyr Pro Val Leu Ser Ser -15 -5 1

His Asp His Asn Ser Leu Gly Leu Leu Ala Asp Lys Val Ala Asn Glu
5 10 15

Ile Asn Arg Ser Asn Cys Arg Val Tyr Ala His Ser His Ser Gly
20 25 30

- (2) INFORMATION FOR SEQ ID NO: 221:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 39 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -32..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.5

seq CLLSXPSTRKSQA/CM

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 221:
- Met Ala Gly Ser Arg Leu Pro Arg Gln Leu Phe Leu Gln Gly Val Xaa
  -30
  -25
  -20

Ala Ser Ser Cys Leu Leu Ser Xaa Pro Ser Thr Arg Lys Ser Gln Ala
-15 -10 -5

Cys Met Ala Pro Arg Ala Trp

- (2) INFORMATION FOR SEQ ID NO: 222:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 35 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -28..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.4 seq FVLHLLAQDLVCC/FY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 222:

Met Tyr Ile Cys Phe Cys Leu Glu Ser Phe Glu Ile Lys Cys Gly Phe
-25 -20 -15

Val Leu His Leu Leu Ala Gln Asp Leu Val Cys Cys Phe Tyr Leu Arg
-10 -5 1

Thr Xaa Xaa 5

- (2) INFORMATION FOR SEQ ID NO: 223:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 35 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -20..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.4

seq LNAFTLLVWLSLS/KN

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 223:

Met His Phe Ile Leu His Asn Leu Asn Ala Phe Thr Leu Leu Val Trp
-20 -15 -10 -5

Leu Ser Leu Ser Lys Asn Thr Val Pro Arg Pro Ala Val Leu Ala Ser
1 5 10

Ala Ala Trp 15

- (2) INFORMATION FOR SEQ ID NO: 224:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 37 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -35..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.2

seq IAPLFTLLPKSIP/AP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 224:

Met Ser Phe Phe Pro Phe Asn Arg Ser Leu Asn Ser Asn Pro His Pro -35 -25 -20

Asn Leu Leu Phe Pro Asn Ile Ala Pro Leu Phe Thr Leu Leu Pro Lys
-15
-5

Ser Ile Pro Ala Pro

- (2) INFORMATION FOR SEQ ID NO: 225:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 54 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -23..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.2

seq LLDLHCFCSLAKT/KN

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 225:
- Met Val Val Trp Val Leu Glu Val Arg Phe Leu Leu Asp Leu His Cys
  -20 -15 -10
- Phe Cys Ser Leu Ala Lys Thr Lys Asn Gly Leu Ser Trp Gly Leu Pro
  -5 1 5
- Gln Lys Val Ala Leu Cys Thr Pro Cys Ser Ala Pro Ala Leu Phe Trp 10 15 20 25
- Phe Gly Phe His Ile Leu

- (2) INFORMATION FOR SEQ ID NO: 226:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 43 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -24..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.2

seq PGLCCPALGSAWS/KN

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 226:
- Met Val Cys Gly Trp Trp Thr Gln Gly Pro Val Pro Gly Leu Cys Cys
  -20 -15 -10
- Pro Ala Leu Gly Ser Ala Trp Ser Lys Asn Lys Ser Xaa Pro Val Pro
  -5 1 5
- Cys Cys Gly Pro Tyr Met Val Ala Asn Leu Gly 10 15
- (2) INFORMATION FOR SEQ ID NO: 227:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 44 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -26..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.2

seq FECALVSASLTTA/GT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 227:

Met Gly Arg Ala Phe Pro Ser Arg His Lys Thr Ala Arg Phe Glu Cys

- ---

-20 -15

Ala Leu Val Ser Ala Ser Leu Thr Thr Ala Gly Thr Pro Gly Lys Asn -5

Leu Xaa Ser Tyr Asn Ser Ala Glu Ala Arg His Ile 10

- (2) INFORMATION FOR SEQ ID NO: 228:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 23 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Placenta
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -18..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5 seq LCXXLLCVLFVSH/FY
    - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 228:

Met Gly Leu Lys Ala Leu Cys Xaa Xaa Leu Leu Cys Val Leu Phe Val

Ser His Phe Tyr Thr Pro Thr 1

- (2) INFORMATION FOR SEQ ID NO: 229:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 94 amino acids
    - (B) TYPE: AMINO ACID
      - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -76..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5 seq FPLLALLFEKCEQ/ST

207

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 229:

Met Met Ala Thr Gln Thr Leu Ser Ile Asp Ser Tyr Gln Asp Gly Gln
-75 -65

Gln Met Gln Val Val Thr Glu Leu Lys Thr Glu Gln Asp Pro Asn Cys
-60 -55 -50 -45

Ser Glu Pro Asp Ala Glu Gly Val Ser Pro Pro Pro Val Glu Ser Gln
-40 -35 -30

Thr Pro Met Asp Val Asp Lys Gln Ala Ile Tyr Arg His Pro Leu Phe
-25 -20 -15

Pro Leu Leu Ala Leu Leu Phe Glu Lys Cys Glu Gln Ser Thr Gln Gly
-10 -5 1

Ser Glu Gly Thr Thr Ser Ala Ser Phe Asp Val Asp Ile Gly
5 10 15

- (2) INFORMATION FOR SEQ ID NO: 230:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 32 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.9 seq SVFLSGSVCLSFL/SE
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 230:

Met Ser Pro Ser Gln Leu Thr Cys Ser Val Phe Leu Ser Gly Ser Val -20 -15 -10

Cys Leu Ser Phe Leu Ser Glu His Arg Thr Tyr Phe Phe Cys Pro Leu
-5 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 231:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 32 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR

. W. ...

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -30..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.8

seq FCSLLCLRTQLFP/HG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 231:

Met Leu Gln Ala Leu Ala Pro Ala His His Leu Cys Ser Leu Lys Arg
-30 -25 -20 -15

Ser Phe Cys Ser Leu Leu Cys Leu Arg Thr Gln Leu Phe Pro His Gly
-10 -5 1

- (2) INFORMATION FOR SEQ ID NO: 232:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 35 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
    - (ix) FEATURE:
      - (A) NAME/KEY: sig\_peptide
      - (B) LOCATION: -14..-1
      - (C) IDENTIFICATION METHOD: Von Heijne matrix
      - (D) OTHER INFORMATION: score 4.8

seq LFLKYLWRSLCRG/GI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 232:

Met Leu Phe Leu Lys Tyr Leu Trp Arg Ser Leu Cys Arg Gly Gly Ile
-10 -5 1

Ile Arg Met Asn His Pro Gly Cys Ser Gln Arg Ile Arg Asp Ser Leu
5 10 15

Cys Asp Leu 20

- (2) INFORMATION FOR SEQ ID NO: 233:
  - (i) SEQUENCE CHARACTERISTICS:

. ....

- (A) LENGTH: 95 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymphocytes
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -37..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.8

seq AILIRPLVSVSGS/GP

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 233:
- Met Ala Leu Leu Ala Met His Ser Trp Arg Trp Ala Ala Ala Ala Ala -35 -30 -25
- Ala Phe Glu Lys Arg Arg His Ser Ala Ile Leu Ile Arg Pro Leu Val -20 -15 -10
- Ser Val Ser Gly Ser Gly Pro Gln Trp Arg Pro His Gln Leu Gly Ala
  -5 1 5 10
- Leu Gly Thr Ala Arg Ala Tyr Gln Ile Pro Glu Ser Leu Lys Ser Ile 15 20 25
- Thr Trp Gln Arg Leu Gly Lys Gly Asn Ser Gly Gln Phe Leu Asp Ala 30 35 40
- Ala Lys Ala Leu Gln Val Trp Pro Leu Ile Glu Lys Arg Thr Trp
  45 50 55
- (2) INFORMATION FOR SEQ ID NO: 234:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 49 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN .
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Placenta
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -38..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.8 seq LASLFGLDQXAAG/HG
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 234:

Met Lys Ala Xaa Ala Met Phe Gly Ala Gly Asp Glu Asp Asp Thr Asp
-35
-25

Phe Leu Ser Pro Ser Gly Gly Ala Arg Leu Ala Ser Leu Phe Gly Leu
-20 -15 -10

Asp Gln Xaa Ala Ala Gly His Gly Asn Xaa Xaa Phe Gln Tyr Thr Ala
-5 1 5 10

Pro-

- (2) INFORMATION FOR SEQ ID NO: 235:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 21 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -13..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.7 seq MLWLLRSLTDVSS/MI
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 235:

Met Leu Trp Leu Leu Arg Ser Leu Thr Asp Val Ser Ser Met Ile Phe
-10 -5 1

Phe Thr Ile Pro Gly

- (2) INFORMATION FOR SEQ ID NO: 236:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 50 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide

. ....

- . (B) LOCATION: -15..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.7 seq IFHVLIAHSSSFS/CE
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 236:

Met Thr Ile Phe His Val Leu Ile Ala His Ser Ser Ser Phe Ser Cys
-15 -5 1

Glu Val Ile Val Lys Val Phe Cys Pro Phe Leu Gly Cys Leu Ser Phe
5 10 15

His Tyr Leu Tyr Ser Leu Leu Glu Phe Phe Ile Leu Asn Thr Ser Pro 20 25 30

Ser Met 35

- (2) INFORMATION FOR SEQ ID NO: 237:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 34 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.7 seq WQLLXGFCGSYSA/AQ
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 237:

Met His Trp Gln Leu Leu Xaa Gly Phe Cys Gly Ser Tyr Ser Ala Ala
-15 -5 1

Gln Ala Glu Ala Gln Thr Leu Pro Gly Leu His Ser Lys Tyr Asn Thr
5 10 15

His Gly

- (2) INFORMATION FOR SEQ ID NO: 238:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 65 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR

THE THE

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -37..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.6

seq FVFLLFFFSXLXY/FM

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 238:

Met Thr Met Met Val Met Ala Ser Phe Leu Pro Arg Asn Thr Met Tyr
-35
-25

Thr Asn Thr Met Asn Tyr Ser Ile Phe Val Phe Leu Leu Phe Phe -20 -15 -10

Ser Xaa Leu Xaa Tyr Phe Met Tyr Lys Thr Ser His Phe Ser Pro Ser -5 1 10

Xaa Ile Cys Tyr Phe Ser Pro Met Xaa Xaa Xaa Xaa Asp Leu Pro Asn 15 20 25

Gly

- (2) INFORMATION FOR SEQ ID NO: 239:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 100 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -61..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.5

seq LVTRLALCQSPRA/GQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 239:

Met Pro Ser Gln Thr Leu Ser Gln Pro Arg Ile Ser Val Leu His Gly
-60 -55 -50

Asp Leu Val Pro Ala Gly Met Ala Val Gln Glu Ile Gly Ala Gln Met
-45 -40 -35 -30

w.E7.

Val Leu Pro Cys Glu Val Val Ser Gly Ser Gly Leu Thr Arg Glu His
-25 -20 -15

Leu Val Thr Arg Leu Ala Leu Cys Gln Ser Pro Arg Ala Gly Gln His
-10 -5 1

Gly Ala Asp Ser Glu Glu Glu Ala Phe Gly Ile Leu Pro Val Arg His
5 10 15

Ser His Arg Leu Ser Ala Cys His Thr Pro Gly Glu Leu Arg Phe Ser 20 25 30 35

Glu Trp Thr Cys

## (2) INFORMATION FOR SEQ ID NO: 240:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 44 amino acids
  - (B) TYPE: AMINO ACID.
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -38..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.5 seq LLMITVTVGPGAS/GV
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 240:

Met Ser Leu Arg Val His Thr Leu Pro Thr Leu Leu Gly Ala Val Val
-35
-30
-25

Arg Pro Gly Cys Arg Glu Leu Leu Cys Leu Leu Met Ile Thr Val Thr

Val Gly Pro Gly Ala Ser Gly Val Cys Pro Ser Gly
-5 5

- (2) INFORMATION FOR SEQ ID NO: 241:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 20 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:

---

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -18..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.5

seq SLLLLGRWLTLTS/SG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 241:

Met Ile Tyr Leu Thr Ser Leu Leu Leu Leu Gly Arg Trp Leu Thr Leu
-15 -10 -5

Thr Ser Ser Gly

- (2) INFORMATION FOR SEQ ID NO: 242:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 24 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -22..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.4

seq GFLLCPLVCGLRR/WT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 242:

Met Asn Trp Asn Val Arg Gly Thr Arg Gly Phe Leu Leu Cys Pro Leu
-20 -15 -10

Val Cys Gly Leu Arg Arg Trp Thr -5 1

- (2) INFORMATION FOR SEQ ID NO: 243:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 44 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

- (vi) · ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -42..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.4

seq LVCLTFITATTHE/QP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 243:

Met Glu Gln Ala Ala Leu Glu Val Val Ser Pro Leu Pro Arg Cys
-40 -35 -30

Ser Val Arg Ser Pro Val Thr Thr Cys Cys Ala Lys Asp Leu Val Cys -25 -20 -15

Leu Thr Phe Ile Thr Ala Thr Thr His Glu Gln Pro

- (2) INFORMATION FOR SEQ ID NO: 244:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 100 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -84..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - · (D) OTHER INFORMATION: score 4.4

seq GLVQLHATXLALG/KV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 244:

Met Ile Ile Pro Leu Pro Ser Leu Val Gly Cys Trp Glu Gly Gly Asn
-80 -75 -70

Gly Lys Gly Leu Met Val Ser Asp Thr Thr Cys Trp Thr Leu Ala Ser
-65 -60 -55

Ser Asn Val Pro Ser Pro Ser Pro Ala Pro Thr Leu Gly Arg Gly Ala
-50 -45 -40

Pro Ser His Thr Pro Gln Lys Lys Pro Thr Ile Pro Gly Ala Arg His
-35 -30 -25

Arg Pro Ile Ile Leu Pro Lys Gly Leu Val Gln Leu His Ala Thr Xaa

PCT/IB98/01237

-20

-15

-10

-5

Leu Ala Leu Gly Lys Val Cys Leu Pro His Val Pro His His Ala Ser 1 5 10

Leu Arg Pro Ala 15

- (2) INFORMATION FOR SEQ ID NO: 245:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 57 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymphocytes
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -42..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.3

seq IQTVHIALPGSLG/HP

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 245:
- Met Ser Met Arg Leu Ser Gly Glu Arg Ile Tyr Leu Leu Glu Val
  -40 -35 -30
- Trp Leu Pro Xaa Leu Asn Phe Glu Ser Val Leu His Phe Ile Gln Thr
  -25 -20 -15
- Val His Ile Ala Leu Pro Gly Ser Leu Gly His Pro Met Gly Pro Cys
  -10 -5 1 5

Ala Cys Arg Pro Ser Leu Ala His Pro 10 15

- (2) INFORMATION FOR SEQ ID NO: 246:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 18 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE: .
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:

w. 2 2

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: -16..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.3 seq LLLFCFMPVVINP/DR
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 246:

Met Gly Thr Leu Leu Phe Cys Phe Met Pro Val Val Ile Asn Pro
-15 -10 -5

Asp Arg

- (2) INFORMATION FOR SEQ ID NO: 247:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 56 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR .
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -22..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1 seq GIYLQLFFLSIVS/QP
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 247:

Met Val Val Leu Asn Pro Met Thr Leu Gly Ile Tyr Leu Gln Leu Phe
-20 -15 -10

Phe Leu Ser Ile Val Ser Gln Pro Thr Phe Ile Asn Ser Val Leu Pro
-5 1 5 10

Ile Ser Ala Ala Leu Pro Ser Leu Asp Gln Lys Lys Arg Gly Gly His
15 20 25

Lys Ala Cys Cys Leu Leu Thr Pro . 30

- (2) INFORMATION FOR SEQ ID NO: 248:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 49 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR

-

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -36..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.1

seq HWLFLASLSGIKT/YQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 248:

Met Ala Pro His Thr Ala Ser Phe Gly Val Cys Pro Leu Leu Ser Val
-35 -30 -25

Thr Arg Val Val Ala Thr Glu His Trp Leu Phe Leu Ala Ser Leu Ser -20 -15 -10 -5

Gly Ile Lys Thr Tyr Gln Ser Tyr Ile Ser Val Phe Cys Lys Val Thr 1 5 10

Gly

- (2) INFORMATION FOR SEQ ID NO: 249:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 23 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -20..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1

seq SLPCLSFCTLCLV/TP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 249:

Met Ser Tyr Lys Trp Met Pro Ser Leu Pro Cys Leu Ser Phe Cys Thr
-20 -15 -10 -5

Leu Cys Leu Val Thr Pro Gly

(2) INFORMATION FOR SEQ ID NO: 250:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 25 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -22..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.1

seq LAGFLLVLYVCLP/HA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 250:

Met Pro Leu Pro Thr Trp Ala Pro Thr Leu Ala Gly Phe Leu Leu Val
-20 -15 -10

Leu Tyr Val Cys Leu Pro His Ala Gly
-5

- (2) INFORMATION FOR SEQ ID NO: 251:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 33 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -17..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1

seg LLDWIGLKALIRG/HD

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 251:
- Met Asn Leu Tyr Leu Leu Asp Trp Ile Gly Leu Lys Ala Leu Ile Arg
- Gly His Asp Ile Lys Ile Gln Ser Leu Cys Pro Ser Pro Cys Leu Pro
  1 5 10 15

Arg

# (2) INFORMATION FOR SEQ ID NO: 252:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 57 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -54..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.1

seq LLLFCFMPVVINP/DX

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 252:

Met Ser Cys Xaa Val Xaa Asp Ala Xaa Xaa Arg Trp Trp Ala His Xaa
-50 -45 -40

Leu Ile Ile Gly Trp Xaa His Leu Thr Gln Lys Val His Pro Ile Ala
-35
-30
-25

Leu Ser His Cys Val Asn Met Gly Thr Leu Leu Leu Phe Cys Phe Met -20 -15 -10

Pro Val Val Ile Asn Pro Asp Xaa Gly
-5

- (2) INFORMATION FOR SEQ ID NO: 253:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 30 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -22..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4

seq ILAFQTFLLNLRA/HL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 253:

Met Val Pro Asn Leu Cys Gly Arg Gln Ile Leu Ala Phe Gln Thr Phe
-20 -15 -10

Leu Leu Asn Leu Arg Ala His Leu Phe Gln Leu Ala Ser Arg
-5 1 5

- (2) INFORMATION FOR SEQ ID NO: 254:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 53 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -14..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4

seq FSLIIFFFPPSSP/XA

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 254:
- Met Phe Ser Leu Ile Ile Phe Phe Phe Pro Pro Ser Ser Pro Xaa Ala
  -10 -5 1
- Asn Pro Phe Pro Ser Tyr Leu Gln Asn Ile Leu Tyr Leu Lys Phe Val 5 10
- His Xaa Ser His Leu Tyr Xaa Xaa Pro Pro Ser Glu Cys Val His Ile 20 25 30

Ser Ser Gly Leu Pro 35

- (2) INFORMATION FOR SEQ ID NO: 255:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 30 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymphocytes
  - (ix) FEATURE:
    - (A) NAME/KÉY: sig\_peptide

- (B) LOCATION: -23..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4 seq LHCLLIVFILVEF/CK
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 255:

Met Ser Ala Phe Tyr Leu Ser Tyr Ser Leu Leu His Cys Leu Leu Ile
-20
-15
-10

Val Phe Ile Leu Val Glu Phe Cys Lys Leu Thr Tyr Phe
-5 1 5

- (2) INFORMATION FOR SEQ ID NO: 256:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 52 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -30..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4 seq SAGVVLTMDGASA/EQ
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 256:

Met Ala Glu Ala Lys Leu Val Gln Gly Ser Leu Val Ala Pro Gln Arg
-30 -25 -20 -15

Xaa Ser Ala Gly Val Val Leu Thr Met Asp Gly Ala Ser Ala Glu Gln
-10 -5 1

Asp Gly Leu Gln Glu Asp Arg Ser His Ser Gly Pro Ser Ser Leu Pro
5 10 15

Glu Ala His Arg 20

- (2) INFORMATION FOR SEQ ID NO: 257:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 74 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -59..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4

seg VLLTISTNASVLG/DG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 257:

Met Lys Gly Val Gly Pro Glu Gln Leu Asn Asp Gly Ala Pro Ser Asn
-55
-50
-45

Glu Ile Glu Met Thr Pro Cys Phe Phe Ser Glu Phe Leu Leu Leu Asp
-40 -35 -30

Val Gly Val Val Asn Ile Val Val Ile Lys Met Ser Tyr Asn Val Leu
-25 -20 -15

Leu Thr Ile Ser Thr Asn Ala Ser Val Leu Gly Asp Gly Ala His Arg
-10 -5 1 5

·Val Thr Thr Arg Ile Arg Arg Pro Gly Gly
10
15

- (2) INFORMATION FOR SEQ ID NO: 258:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 70 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -45..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8

seq QLFWVTASTFCRS/DI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 258:

Met Leu Arg Lys Leu Ser Ala Ser Asn Glu Asn Leu Cys Leu Leu Ser -45 -35 -30

Asn Pro Ser His Asn Glu Val Tyr Leu Ile Arg Cys Cys Glu Ser His
-25 -20 -15

Gln Leu Phe Trp Val Thr Ala Ser Thr Phe Cys Arg Ser Asp Ile Ala
-10 -5 1

Thr Met Ala Ser Leu Leu Pro Ser Val Leu Leu Met Gln Leu Phe Ser 5 10 15

Thr Phe Phe Leu Asn Leu 20 25

---

- (2) INFORMATION FOR SEQ ID NO: 259:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 18 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8 seq PLILLPLNPFVLQ/VA
      - .
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 259:

Met Tyr Pro Leu Ile Leu Leu Pro Leu Asn Pro Phe Val Leu Gln Val -15 -5 1

Ala Gly

- (2) INFORMATION FOR SEQ ID NO: 260:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 67 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -23..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8 seq RGFVAVGLGQISA/SP

WAS LET THE

(xi) .SEQUENCE DESCRIPTION: SEQ ID NO: 260:

Met Leu Leu Arg Pro Ser Pro Gly Ser Pro Arg Gly Phe Val Ala Val -20 -15 -10

Gly Leu Gly Gln Ile Ser Ala Ser Pro Ser Met Ala Cys Lys Leu Thr
-5 1 5

Ile Leu Gln His Thr Ser Val Phe Arg Val Val Phe Arg Thr Pro
10 15 20 25

Leu Val Arg Gly Pro Leu Ser Arg Ser Asn Glu Leu Trp Leu His His 30 35 40

Leu Ser Ser

- (2) INFORMATION FOR SEQ ID NO: 261:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 25 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
    - (ii) MOLECULE TYPE: PROTEIN
    - (vi) ORIGINAL SOURCE:
      - (A) ORGANISM: Homo Sapiens
      - (F) TISSUE TYPE: Umbilical cord
    - (ix) FEATURE:
      - (A) NAME/KEY: sig\_peptide
      - (B) LOCATION: -18..-1
      - (C) IDENTIFICATION METHOD: Von Heijne matrix
      - (D) OTHER INFORMATION: score 3.8 seq ATACGPAAHQCSA/VP
    - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 261:

Met Ala Arg Pro Gly Ala Thr Ala Cys Gly Pro Ala Ala His Gln Cys
-15
-10
-5

Ser Ala Val Pro Leu Trp Ser Pro Gly

- (2) INFORMATION FOR SEQ ID NO: 262:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 23 amino acids
    - (B) TYPE: AMINO ACID
      (D) TOPOLOGY: LINEAR
    - •
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Umbilical cord

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: -19..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.8

seq LSLCIXXLEHLFT/WP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 262:

Met Glu Pro Val Ser Ser Leu Ser Leu Cys Ile Xaa Xaa Leu Glu His
-15 -10 -5

Leu Phe Thr Trp Pro Lys Gly

- (2) INFORMATION FOR SEQ ID NO: 263:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 28 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8

seq WCSAAAWRSPLSA/AT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 263:

Met Arg Pro Ala Gly Arg Trp Cys Ser Ala Ala Ala Trp Arg Ser Pro
-15 -5

Leu Ser Ala Ala Thr Leu Lys Cys Pro Leu Arg Gly
1 5

- (2) INFORMATION FOR SEQ ID NO: 264:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 19 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:

---

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -16..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.7

seq CAYVLFFFNGCLY/RR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 264:

Met Trp Leu Cys Ala Tyr Val Leu Phe Phe Phe Asn Gly Cys Leu Tyr
-15
-5

Arg Arg Lys

- (2) INFORMATION FOR SEQ ID NO: 265:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 46 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6

seq LLHRAVVLRLQQA/CR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 265:

Met Leu Leu His Arg Ala Val Val Leu Arg Leu Gln Gln Ala Cys
-15 -5 1

Arg Pro Thr Ser Leu Pro Asp Ser Ser Gln Ser Pro Gln Gly Ser Ala
5 10 15

Phé Arg Pro Ala Pro Gln Met Ile His Phe Ser Pro Leu Xaa 20 25 30

- (2) INFORMATION FOR SEQ ID NO: 266:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 53 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -32..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.6

seq SLVPSMCFHVTNS/IK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 266:

Met Glu Met Phe Gly Xaa Xaa Glu Lys Asp Phe Ser Ser Val Glu Gly
-30 -25 -20

Val Leu Xaa Ser Leu Val Pro Ser Met Cys Phe His Val Thr Asn Ser -15 -10 -5

Ile Lys Met Pro Trp Phe Pro Ser Gln Pro Gly Thr Cys Thr Gln Lys
1 5 10 15

Asp Cys Pro Pro Lys
20

- (2) INFORMATION FOR SEQ ID NO: 267:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 48 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -46..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6 seq LLGVHASFQMSVA/AR
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 267:
- Met Gln Met His Gly Trp Arg Trp Asp Pro His Ser Ser Glu Gln Leu
  -45 -40 -35
- Asp Leu Ala His Thr Leu Ser Arg Glu Ala Ser Leu Glu Asn Asn Thr
  -30 -25 -20 -15
- Ala Leu Leu Gly Val His Ala Ser Phe Gln Met Ser Val Ala Ala Arg

1

-5

(2) INFORMATION FOR SEQ ID NO: 268:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 37 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymphocytes
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -34..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.6

seq VGTGVLTSRLARA/TP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 268:

Met Ala Ser Pro Arg Gly Thr Asp Tyr Asn Gln Thr Pro Asn Thr Thr
-30 -25 -20

Met Tyr Cys Tyr Ala Val Gly Thr Gly Val Leu Thr Ser Arg Leu Ala
-15 -10 -5

Arg Ala Thr Pro Gly
1

- (2) INFORMATION FOR SEQ ID NO: 269:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 71 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymphocytes
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LCCATION: -42..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6

seq LHCLCPFPALFLS/VT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 269:

Met Ala Pro Ile Leu Ser Ser Phe Lys Ser Leu Leu Lys Tyr His Leu
-40 -35 -30

Leu Glu Thr Ser Leu Ser Ile Leu Leu Lys Pro Val Thr Leu His Cys
-25
-20
-15

Leu Cys Pro Phe Pro Ala Leu Phe Leu Ser Val Thr Phe Ile Tyr Leu -10 -5 1 5

Thr Tyr Tyr Ile Phe Asn Leu Tyr Ile Leu Phe Ile Val Cys Leu Leu
10 15 20

Tyr Trp Asn Val Leu Ser Met

- (2) INFORMATION FOR SEQ ID NO: 270:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 31 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -22..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.5 seq ILVPWWLPPFVYT/AI
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 270:

Met Asn Arg Leu Ser Lys His Leu Ile Ile Leu Val Pro Trp Leu
-20 -15 -10

Pro Pro Phe Val Tyr Thr Ala Ile Ser Tyr Val Gln Leu Pro Gly
-5 5

- (2) INFORMATION FOR SEQ ID NO: 271:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 32 amino acids
    - (3) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -29..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.5

seq ALITILILYSSNS/AI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 271:

Met Ser Ser Asn Lys Glu Gln Arg Ser Ala Val Phe Val Ile Leu Phe
-25 -20 -15

Ala Leu Ile Tnr Ile Leu Ile Leu Tyr Ser Ser Asn Ser Ala Ile Gly
-10 -5 1

- (2) INFORMATION FOR SEQ ID NO: 272:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 73 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymphocytes
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -68..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.5

seq CLFLSPQSFLVLS/WA

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 272:
- Met Asp Met Lys Ser Asn Thr Gly His Gly Leu Phe Leu Gly Arg Gln
  -65 -60 -55
- Pro Ser Phe Ser Val Arg Ser Met Pro Gly Thr Pro Ala Leu Ala Ile
  -50 -45 -40
- Cys Gln Pro His Asn Pro Gly Pro Pro Met Gly Thr Pro Thr Glu Asp -35 -30 -25
- Pro Ser Gly Cys Ser Phe Pro Cys Leu Phe Leu Ser Pro Gln Ser Phe
  -20 -15 -10 -5

Leu Val Leu Ser Trp Ala Ile Ser Arg

- (2) INFORMATION FOR SEQ ID NO: 273:
  - (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 36 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -29..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.5

seq LSLSSTLLLTSHH/HQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 273:

Met Ser Glu Ala Gly Cys Lys Pro Ser Arg Pro Glu His Gly Ser Phe
-25
-20
-15

Leu Ser Leu Ser Ser Thr Leu Leu Leu Thr Ser His His Gln Ser
-10 -5 1

Ser Asp Phe Gly

- (2) INFORMATION FOR SEQ ID NO: 274:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 114 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 12.8

seq XVFLVALLRGVQC/QV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 274:

Met Glu Ser Gly Xaa Gly Xaa Val Phe Leu Val Ala Leu Leu Arg Gly
-15 -10 -5

Val Gln Cys Gln Val Gln Ile Val Gln Ser Gly Gly Val Val Gln
1 5 10

Pro Gly Lys Ser Gln Thr Leu Ser Cys Val Thr Tyr Gly Phe Arg Phe

25

15

Asp Asp Phe Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 30 35 40 45

20

Glu Trp Val Ala Met Ile Arg Tyr Asp Gly Ser Asn Lys Phe Tyr Ser 50 55 60

Lys Ser Val Gln Gly Arg Phe Leu Ile Ser Arg Asp Asn Ser Arg Asn 65 70 75

Gln Val Tyr Leu Ser Leu Asn Arg Leu Arg Val Asp Asp Thr Ala Val 80 85 90

Tyr Tyr 95

- (2) INFORMATION FOR SEQ ID NO: 275:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 26 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -17..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 9.3 seq LFTLLLLQSLLLG/CC
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 275:

Met Leu Cys Arg Leu Phe Thr Leu Leu Leu Gln Ser Leu Leu Leu -15 -5

Gly Cys Cys Ile Tyr Xaa Pro Gly Asn Gly

- (2) INFORMATION FOR SEQ ID NO: 276:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 97 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens

---

(F) TISSUE TYPE: Lymph ganglia

### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: -26..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 9.3

seq FLLLVAGPRWVLS/QV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 276:

Met Asp Leu Leu His Lys Asn Met Lys His Leu Trp Phe Phe Leu Leu -25 -20 -15

Leu Val Ala Gly Pro Arg Trp Val Leu Ser Gln Val Arg Leu Glu Gln -10 -5 1 5

Trp Gly Ser Gly Leu Val Lys Ser Ser Glu Thr Leu Ser Leu Thr Cys
10 15 20

Ala Val Tyr Gly Gly Ser Ala Ile Ser Asp Tyr Trp Ala Trp Ile Arg
25 30 35

Gln Phe Pro Gly Lys Gly Val Glu Trp Ile Gly Glu Ile Asn His Ser 40 45 50

Gly Ala Thr His Tyr Ile Arg Pro Ser Gly Val Glu Ser Pro Ser Pro 55 60 65 70

Leu

- (2) INFORMATION FOR SEQ ID NO: 277;
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 77 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (li) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -51..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.1

seq VCLCGTFCFPCLG/CQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 277:

Met Gln Ala Gln Ala Pro Val Val Val Thr Gln Pro Gly Val Gly
-50 -45 -40

Pro Gly Fro Ala Pro Gln Asn Ser Asn Trp Gln Thr Gly Met Cys Asp

-35 -30 -25 -20

Cys Phe Ser Asp Cys Gly Val Cys Leu Cys Gly Thr Phe Cys Phe Pro
-15 -10 -5

Cys Leu Gly Cys Gln Val Ala Ala Asp Met Asn Glu Cys Cys Leu Cys
1 5 10

Gly Thr Ser Val Ala Met Arg Thr Leu Xaa Arg Xaa Arg 15 20 25

- (2) INFORMATION FOR SEQ ID NO: 278:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 52 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymphocytes
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -18..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.7 seq LLLLPVLGLLVSS/KT
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 278:

Met Lys Ala Leu Cys Leu Leu Leu Pro Val Leu Gly Leu Leu Val
-15 -10 -5

Ser Ser Lys Thr Leu Cys Ser Met Glu Glu Ala Ile Asn Glu Arg Ile 1 5 10

Gin Glu Val Ala Gly Ser Leu Ile Phe Arg Ala Ile Ser Ser Ile Gly
15 20 25 30

Arg Gly Ser Glu

- (2) INFORMATION FOR SEQ ID NO: 279:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 59 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -21..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.6

seq LLXIVGLXLPTXG/QX

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 279:
- Met Ser Pro Ser Gly Arg Leu Cys Leu Leu Xaa Ile Val Gly Leu Xaa -20 -15 -10

Leu Pro Thr Xaa Gly Gln Xaa Leu Lys Asp Thr Xaa Ser Ser Ser Ser -5 10

Ala Asp Ser Thr Ile Met Asp Ile Gln Val Pro Thr Arg Ala Pro Asp
15 20 25

Ala Val Tyr Thr Glu Leu Gln Pro Thr His Gly 30 35

- (2) INFORMATION FOR SEQ ID NO: 280:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 56 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.2 seq FLVSNMLLAEAYG/SG
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 280:
- Met Leu Leu Ala Trp Val Gln Ala Phe Leu Val Ser Asn Met Leu Leu -20 -15
- Ala Glu Ala Tyr Gly Ser Gly Gly Cys Phe Trp Asp Asn Gly His Leu
  -5 1 5 10
- Tyr Arg Glu Asp Gln Thr Ser Pro Ala Pro Gly Leu Arg Cys Leu Asn
  15 20 25
- Trp Leu Asp Ala Gln Asn Gly Leu
  30 35

- (2) INFORMATION FOR SEQ ID NO: 281:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 132 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -62..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.8

seg LXLTCSVSGGSIS/RT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 281:

Met Leu Ser Glu Ser Arg Gly Pro Pro Val Gln Glu His Glu Ala Pro
-60 -55 -50

Val Val Leu Pro Pro Ala Gly Gly Gly Ser Gln Met Gly Pro Val Pro
-45 -40 -35

Ala Ala Xaa Ala Gly Glu Ser Gly Pro Gly Xaa Val Lys Pro Leu Glu
-30 -25 -20 -15

Thr Leu Xaa Leu Thr Cys Ser Val Ser Gly Gly Ser Ile Ser Arg Thr
-10 -5 1

Ser Phe Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
5 10 15

Trp Ile Gly Ser Ile Tyr Asp Xaa Gly Ser Thr Tyr Tyr Asn Pro Ser
20 25 30

Leu Xaa Xaa Xaa Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Val 35 40 45 50

Ser Leu Lys Val Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr His
55 60 65

Cys Ala Arg Gly 70

- (2) INFORMATION FOR SEQ ID NO: 282:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 137 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

WO 99/06553 PCT/IB98/01237

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -108..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.3

seq ACMTLTASPGVFP/SL

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 282:
- Met Thr Ser Gly Gln Ala Arg Ala Ser Xaa Gln Ser Pro Gln Ala Leu
  -105 -100 -95
- Glu Asp Ser Gly Pro Val Asn Ile Ser Val Ser Ile Thr Leu Thr Leu
  -90 -85 -80
- Asp Pro Leu Lys Pro Phe Gly Gly Tyr Ser Arg Asn Val Thr His Leu
  -75 -70 -65
- Tyr Ser Thr Ile Leu Gly His Gln Ile Gly Leu Ser Gly Arg Glu Ala
  -60 -55 -50 -45
- His Glu Glu Ile Asn Ile Thr Phe Thr Leu Pro Thr Ala Trp Ser Ser -40 -35 -30
- Asp Asp Cys Ala Leu His Gly His Cys Glu Gln Val Val Phe Thr Ala
  -25
  -20
  -15
- Cys Met Thr Leu Thr Ala Ser Pro Gly Val Phe Pro Ser Leu Tyr Ser
  -10 -5 1
- His Arg Thr Val Phe Leu Thr Arg Thr Ala Thr Pro Arg Ser Gly Thr 5 10 15 20

Arg Ser Ser Gln Leu Pro Glu Met Pro 25

- (2) INFORMATION FOR SEQ ID NO: 283:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 48 amino acids
      - (B) TYPE: AMINO ACID
      - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix

- (D) OTHER INFORMATION: score 5.1 seq LLLKIWLLQRPES/QE
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 283:
- Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu -20 -15 -10
- Gin Arg Pro Glu Ser Gin Glu Gly Leu Leu Pro Gly Arg Leu Val Val -5 10
- Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Ala 15 20 25
- (2) INFORMATION FOR SEQ ID NO: 284:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 56 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -29..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.6

seq SLMSLLDESSCQA/VG

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 284:
- Met Arg Phe Arg Lys Ala Trp Ala Pro Val Leu Ala Ala Leu Ser His
   -25 -20 -15
- Ser Leu Met Ser Leu Leu Asp Glu Ser Ser Cys Gln Ala Val Gly Arg
  -10 -5 1
- Pro Val Glu Lys Leu Ala Arg Asn Trp Trp Gly Pro Phe Pro Pro Ile
  5 10 15
- Ala Ser Lys Glu Leu Asn Pro Ala 20 25
- (2) INFORMATION FOR SEQ ID NO: 285:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 105 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR

- Tarabana - Tarabana

- (ii) MOLECULE TYPE: PROTEIN -
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -82..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.4

seq NLPHLQVVGLTWG/HI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 285:

Met Tyr Val Trp Pro Cys Ala Val Val Leu Ala Gln Tyr Leu Trp Phe
-80 -75 -70

His Arg Arg Ser Leu Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala Gly
-65 -60 -55

Val Ser Leu Pro Gly Ile Leu Ala Ala Lys Cys Gly Ala Glu Val Ile
-50 -45 -40 -35

Leu Ser Asp Ser Ser Glu Leu Pro His Cys Leu Glu Val Cys Arg Gln
-30 -25 -20

Ser Cys Gln Met Asn Asn Leu Pro His Leu Gln Val Val Gly Leu Thr
-15 -10 -5

Trp Gly His Ile Ser Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp Ile
1 5 10

Ile Leu Ala Ser Asp Val Phe Phe Glu

- (2) INFORMATION FOR SEQ ID NO: 286:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 126 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -56..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.4 seq LWKLALQSSSCLS/LF
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 286:

Met Leu Asn Pro Ala Gln Xaa Asp Thr Met Pro Cys Glu Tyr Leu Ser -55 -50 -45

Leu Asp Ala Met Glu Lys Trp Ile Ile Phe Gly Phe Ile Leu Cys His
-40 -35 -30 -25

Gly Ile Leu Asn Thr Xaa Ala Thr Ala Leu Asn Leu Trp Lys Leu Ala
-20 -15 -10

Leu Gln Ser Ser Cys Leu Ser Leu Phe Arg Asp Glu Val Phe His
-5 1 5

Ile His Lys Ala Ala Glu Asp Leu Phe Val Asn Ile Arg Gly Tyr Asn 10 15 20

Lys Arg Ile Asn Asp Ile Arg Glu Cys Lys Xaa Ala Ala Val Ser His 25 30 35 40

Ala Gly Ser Met His Arg Glu Arg Arg Lys Xaa Leu Arg Ser Ala Leu
45 50 55

Lys Glu Leu Ala Thr Val Leu Ser Asp Gln Pro Gly Leu Leu 60 65 70

### (2): INFORMATION FOR SEQ ID NO: 287:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 27 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -24..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.9 seq GVCLSVPSLPSIS/RP
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 287:

Met Asn Ala Gln Ala Ser Ser Ser Arg Cys His Gly Val Cys Leu Ser
-20 -15 -10

Val Pro Ser Leu Pro Ser Ile Ser Arg Pro Pro
-5 1

- (2) INFORMATION FOR SEQ ID NO: 288:
  - (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 74 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Umbilical cord
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -67..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.8

seq QVLDSVLVGPVPA/ER

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 288:

Met Ala Lys Val Gln Val Asn Asn Val Val Leu Asp Asn Pro Ser
-65 -60 -55

Pro Phe Tyr Asn Pro Phe Gln Phe Glu Ile Thr Phe Glu Cys Ile Glu -50 -45 -40

Asp Leu Ser Glu Asp Leu Glu Trp Lys Ile Ile Tyr Val Gly Ser Ala
-35 -25 -20

Glu Ser Glu Glu Tyr Asp Gln Val Leu Asp Ser Val Leu Val Gly Pro
-15 -10 -5

Val Pro Ala Glu Arg His Met Phe Val Phe 1 5

- (2) INFORMATION FOR SEQ ID NO: 289:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 38 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymphocytes
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.7

seq ETCALASHSGSSG/SK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 289:

Met Ala Asp Val Glu Asp Gly Glu Glu Thr Cys Ala Leu Ala Ser His

-15 -10

Ser Gly Ser Ser Gly Ser Lys Ser Gly Gly Asp Lys Met Phe Ser Leu

Lys Lys Trp Asn Ala Val 15

- (2) INFORMATION FOR SEQ ID NO: 290:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 22 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -14..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.5 seq WTCLLGDCGPPEA/FT
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 290:

Met Trp Thr Cys Leu Leu Gly Asp Cys Gly Pro Pro Glu Ala Phe Thr

Ser Tyr Gln Pro Pro Arg 5

- (2) INFORMATION FOR SEQ ID NO: 291:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 70 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 11.7

seq VFCLLAVAPGAHS/QV

**WO 99/06553** 

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 291:

Met Asp Trp Thr Trp Xaa Val Phe Cys Leu Leu Ala Val Ala Pro Gly
-15 -10 -5

Ala His Ser Gln Val Gln Leu Val Gln Ser Xaa Ala Xaa Val Arg Xaa
1 5 10

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Pro Ser Gly Tyr Ser Phe 15 20 25

Thr Ser His Tyr Val His Trp Val Arg Xaa Asp Pro Gly Gln Xaa Leu 30 45

Glu Trp Met Gly Asp Gly 50

- (2) INFORMATION FOR SEQ ID NO: 292:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 75 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -33..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 10.9 seq LVSLLLLLTRVQP/GT
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 292:

Met Asp Asn Ser Trp Arg Leu Gly Pro Ala Ile Gly Leu Ser Ala Gly
-30 -25 -20

Gln Ser Gln Leu Leu Val Ser Leu Leu Leu Leu Leu Thr Arg Val Gln
-15 -10 -5

Pro Gly Thr Asp Val Ala Ala Pro Glu His Ile Ser Tyr Val Pro Gln
1 5 10 15

Leu Ser Asn Asp Thr Leu Ala Gly Arg Leu Thr Leu Ser Thr Phe Thr 20 25 30

Leu Glu Gln Pro Leu Gly Gln Phe Ser Ser Arg
35 40

(2; INFORMATION FOR SEQ ID NO: 293:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 95 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -19..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 10.9

seq FLLLVAAPRWVLS/QV

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 293:
- Met Xaa His Leu Xaa Phe Phe Leu Leu Val Ala Ala Pro Arg Trp
  -15 -10 -5
- Val Leu Ser Gln Val Leu Leu Gln Glu Ser Gly Pro Glu Leu Val Lys
  1 5 10
- Pro Ser Xaa Thr Leu Ser Leu Thr Xaa Ala Val Ser Gly Gly Ser Ile 15 20 25
- Ser Gly Gly Pro Tyr Tyr Trp Asn Trp Val Xaa Gln His Pro Gly Lys 30 35 40 45
- Gly Leu Glu Xaa Ile Gly Asn Ile Tyr Tyr Asn Gly Ser Thr Phe Xaa 50 55 60
- Xaa Pro Val Pro Gln Xaa Ser Xaa Tyr His Ile Xaa Arg Arg Arg 65 70 75
- (2) INFORMATION FOR SEQ ID NO: 294:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 85 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -28..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 9.6 seq LLTLLLGLTEVAG/EE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 294:

Met Pro Val Pro Ala Ser Trp Pro His Pro Pro Gly Pro Phe Leu Leu
-25 -20 -15

Leu Thr Leu Leu Gly Leu Thr Glu Val Ala Gly Glu Glu Leu
-10 -5 1

Gln Met Ile Gln Pro Glu Lys Leu Leu Leu Val Thr Val Gly Lys Thr 5 10 15 20

Ala Thr Leu His Cys Thr Val Thr Ser Leu Leu Pro Val Gly Pro Val 25 30 35

Leu Trp Phe Arg Gly Val Gly Pro Gly Arg Glu Leu Ile Tyr Asn Gln
40 45 50

Lys Glu Gly Leu Xaa 55

- (2) INFORMATION FOR SEQ ID NO: 295:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 38 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 9.6 seq EYVLLFLALCSA/KP
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 295:

Met Lys Glu Tyr Val Leu Leu Leu Phe Leu Ala Leu Cys Ser Ala Lys
-15 -5 1

Pro Phe Phe Ser Pro Ser His Ile Ala Leu Lys Asn Met Met Leu Lys
5 10 15

Asp Met Glu Asp Thr Glu 20

- (2) INFORMATION FOR SEQ ID NO: 296:
  - (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 39 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -17..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9.3

seq LALSLLILVLAFG/IP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 296:

Met Ala Gln Ser Leu Ala Leu Ser Leu Leu Ile Leu Val Leu Ala Phe
-15
-10
-5

Gly Ile Pro Arg Thr Gln Gly Ser Asp Gly Gly Ala Gln Asp Cys Cys
1 5 10 15

Leu Lys Tyr Ser Gln Thr Arg

- (2) INFORMATION FOR SEQ ID NO: 297:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 83 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -17..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.2

seq LLLITAILAVAVG/FP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 297:

Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val -15 -10 -5

Gly Phe Pro Val Ser Gln Asp Xaa Glu Arg Glu Lys Arg Ser Ile Ser 1 5 10 15

Asp Ser Asp Glu Leu Ala Ser Gly Phe Phe Val Phe Pro Tyr Pro Tyr

20

25

Pro Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe 35 40 45

Arg Arg Asn Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Thr Thr Pro
50 55 60

Leu Pro Met 65

- (2) INFORMATION FOR SEQ ID NO: 298:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 78 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -17..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.2

seq LLLITAILAVAVG/FP

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 298:
- Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val -15 -10 -5
- Gly Phe Pro Val Ser Gln Asp Gln Glu Arg Glu Lys Arg Ser Ile Ser 1 5 10 15
- Asp Ser Asp Glu Leu Ala Ser Gly Xaa Phe Val Phe Pro Tyr Pro Tyr 20 25 30
- Pro Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe 35 40 45
- Arg Arg Xaa Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Gly
  50 55 60
- (2) INFORMATION FOR SEQ ID NO: 299:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 51 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Placenta
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -18..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.1

seq LFTAILAFSLAQS/FG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 299:

Met Arg Ile Met Leu Leu Phe Thr Ala Ile Leu Ala Phe Ser Leu Ala
-15 -10 -5

Gln Ser Phe Gly Ala Val Cys Lys Glu Pro Gln Glu Glu Val Val Pro

1 5 10

Gly Gly Arg Ser Lys Arg Asp Pro Asp Leu Tyr Gln Leu Leu Gln
15 20 25 30

Arg Pro Trp

- (2) INFORMATION FOR SEQ ID NO: 300:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 125 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
    - (vi) ORIGINAL SOURCE:
      - (A) ORGANISM: Homo Sapiens
      - (F) TISSUE TYPE: Lymph ganglia
    - (ix) FEATURE:
      - (A) NAME/KEY: sig\_peptide
      - (B) LOCATION: -17..-1
      - (C) IDENTIFICATION METHOD: Von Heijne matrix
      - (D) OTHER INFORMATION: score 7.9

seq VLLLGLLSHCTVS/VS

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 300:
- Met Ala Trp Thr Val Leu Leu Gly Leu Leu Ser His Cys Thr Val
- Ser Val Ser Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala 1 5 10 15
- Pro Gly Glu Thr Ala Thr Ile Ser Cys Gly Ala Asn Asn Val Gly Arg
- Lys Asn Val Gln Trp Tyr Gln Gln Lys Ala Gly Gln Ala Pro Val Leu

---

35

40

Val Ile Tyr His Asp Val Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe 50 55 60

Ser Gly Ser Asn Ser Gly Ser Pro Ala Lys Leu Thr Ile Ser Arg Val 65 70 75

Glu Ala Gly Asp Glu Ala Asp Tyr Xaa Cys Xaa Val Trp Asp Ser Asp 80 95

Ser Asp His Thr Val Ile Phe Gly Gly Gly Thr Lys Leu 100 105

# (2) INFORMATION FOR SEQ ID NO: 301:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 82 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -58..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.7

seq PXLLLQTLPASTX/XP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 301:

Met Thr Ile Leu His Thr Gly Xaa Asn Pro Phe Arg Pro Ser Gln Arg
-55 -50 -45

Trp Thr Ala Pro Ala Leu Leu His His Arg Pro Xaa Thr Xaa Pro Pro
-40 -35 -30

Ser Xaa His Arg Ser Arg Cys Thr Glu Xaa Val Gly Ile Pro Xaa Leu
-25 -20 -15

Leu Leu Gln Thr Leu Pro Ala Ser Thr Xaa Xaa Pro Gln Ala Phe Arg
-10 -5 1 5

Arg Xaa Ser Asp Pro Pro Ala Lys Pro Pro Gln Ile Tyr Tyr Arg Val
10 15 20

Gln His

- (2) INFORMATION FOR SEQ ID NO: 302:
  - (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 115 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -20..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.2

seq LLLLVAAPKXXLS/QV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 302:

Met Lys His Leu Trp Phe Phe Leu Leu Leu Leu Val Ala Ala Pro Lys
-20 -15 -10 -5

Xaa Xaa Leu Ser Gln Val Gln Leu Arg Glu Ser Gly Pro Gly Leu Val 1 5 10

Glu Pro Ser Gln Thr Leu Ser Leu Thr Cys Ser Val Ser Arg Gly Ser 15 20 25

Val Asn Ser Gly Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly 30 35 40

Lys Gly Leu Glu Trp Ile Gly Tyr Val Tyr Tyr Gly Gly Xaa Thr Tyr 45 50 55 60

Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Leu Ser Ala Asp Thr Ser
65 70 75

Lys Asn Gln Phe Phe Leu Arg Leu Thr Ser Met Thr Ala Ala Asp Thr 80 85 90

Ala Ser Gly

- (2) INFORMATION FOR SEQ ID NO: 303:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 43 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide

- (B) LOCATION: -21..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.9 seq LVCGSLGLSNVSG/IY
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 303:

Met Leu Ser Tyr Phe Leu Ser Ser Leu Val Cys Gly Ser Leu Gly Leu
-20 -15 -10

Ser Asn Val Ser Gly Ile Tyr Asp Ser Lys Lys Lys Arg Lys Thr Gly
-5 1 5 10

Ala Phe Arg Thr Gln Leu Phe Trp Gly Val Gly
15 20

- (2) INFORMATION FOR SEQ ID NO: 304:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 57 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -42..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.4 seq ELPALALLHAGHA/EP
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 304:

Met Gly Thr Gln Asp Pro Gln Ala Glu Gln Gly Leu Arg Ile Pro Leu
-40 -35 -30

Pro Gly Leu Leu Ser Lys His His Pro Ala Pro Glu Leu Pro

Ala Leu Ala Leu Leu His Ala Gly His Ala Glu Pro Ala Gln Asp Gly -10 -5 1 5

Glu Pro Gly His Pro Arg Gly Pro Gly
10 15

- (2) INFORMATION FOR SEQ ID NO: 305:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 76 amino acids
    - (B) TYPE: AMINO ACID

- . (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -33..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.3

seq SXXPLXSVQLXHA/QR

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 305:
- Met Met Thr Ile Tyr Ala Leu Ser Asn Glu Phe Ala Phe Lys Ile Asn
  -30
  -25
  -20
- Glu Glu Gln Leu Ser Xaa Xaa Pro Leu Xaa Ser Val Gln Leu Xaa His
  -15 -10 -5
- Ala Gln Arg Phe Leu Leu Asp Ser Ser Trp Ser Gly Val Ile Pro Phe 1 5 10 15
- Phe Phe Ser Cys Ser Cys Leu Pro Phe Leu Tyr Pro Pro Lys Trp Arg 20 25 30
- Gln Ile His Asp Leu Lys Asp Thr Gln Tyr Arg Ser 35 40
- (2) INFORMATION FOR SEQ ID NO: 306:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 26 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymphocytes
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.1

seq LEMLTAFASHIRA/RD

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 306:
- Met Arg Gly Ala His Leu Xaa Ala Leu Glu Met Leu Thr Ala Phe Ala

Ser His Ile Arg Ala Arg Asp Ala Ala Arg -5 1 5

- (2) INFORMATION FOR SEQ ID NO: 307:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 71 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -52..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.1

seq IILLIHTMQVCTT/HP

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 307:
- Met Asn Pro Glu Ser Pro Gln Gln Leu Glu Arg Gln Ser Thr Gly Pro
  -50 -45 -40
- Arg Thr Gly Thr Arg Arg Cys Leu Ser Lys Phe Thr Trp Cys Thr Ser
  -35 -30 -25
- Arg Met Met Thr Gln Thr Cys Ile Ile Leu Leu Ile His Thr Met Gln -20 -15 -10 -5
- Val Cys Thr His Pro Thr Val Leu Ser His Thr Leu Leu Gln Arg

  1 5 10

Pro Lys Pro Thr Asp Pro Arg

- (2) INFORMATION FOR SEQ ID NO: 308:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 33 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord-
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -19..-1

- ---

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.1 seq IILLIHTMQVCTT/HP
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 308:

Met Met Thr Gln Thr Cys Ile Ile Leu Leu Ile His Thr Met Gln Val

Cys Thr Thr His Pro Thr Val Leu Ser His Thr Leu Leu Gln Arg Pro 1 5 10

Met

- (2) INFORMATION FOR SEQ ID NO: 309:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 82 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -25..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6

seq LLGLLVAVATVHL/VI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 309:

Met Ala Gly Lys Gly Ser Ser Gly Arg Arg Pro Leu Leu Cly Leu -25 -15 -10

Leu Val Ala Val Ala Thr Val His Leu Val Ile Cys Pro Tyr Thr Lys
-5 1 5

Val Glu Glu Ser Phe Asn Leu Gln Ala Thr His Asp Leu Leu Tyr His
10 20

Trp Gln Asp Leu Glu Gln Tyr Asp His Leu Glu Phe Pro Gly Val Val 25 30 35

Pro Arg Thr Xaa Leu Gly Pro Val Val Ile Ala Val Phe Ser Ser Pro 40 45 50 55

Ala Val

(2) INFORMATION FOR SEQ ID NO: 310:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 124 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -22..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.9

seq LIYILWQLTGSAA/SG

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 310:
- Met Ala Gly Ser Pro Thr Cys Leu Thr Leu Ile Tyr Ile Leu Trp Gln
  -20 -15 -10
- Leu Thr Gly Ser Ala Ala Ser Gly Pro Val Lys Glu Leu Val Gly Ser
  -5 1 1 5 10
- Val Gly Gly Ala Val Thr Phe Pro Leu Lys Ser Lys Val Lys Gln Val 15 20 25
- Asp Ser Ile Val Trp Thr Phe Asn Thr Thr Pro Leu Val Thr Ile Gln
  30 35 40
- Pro Glu Gly Gly Xaa Ile Ile Val Thr Gln Asn Arg Asn Arg Glu Arg
  45 50 55
- Val Asp Phe Pro Asp Gly Gly Tyr Ser Leu Lys Leu Ser Lys Leu Lys
  60 65 70
- Lys Asn Asp Ser Xaa Ile Tyr Tyr Val Gly Ile Tyr Ser Ser Leu
  75 80 85 90
- Gln Gln Pro Xaa Thr Gln Glu Tyr Val Leu His Val 95 100
- (2) INFORMATION FOR SEQ ID NO: 311:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 21 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:

-

- . (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -18..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.8

seq CFIILGLIICIQC/ST

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 311:

Met Val Gly Met Val Cys Phe Ile Ile Leu Gly Leu Ile Ile Cys Ile
-15
-10
-5

Gln Cys Ser Thr Gly

- (2) INFORMATION FOR SEQ ID NO: 312:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 116 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -13..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.7

seq MXLLHSLSSGVRA/PS

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 312:
- Met Xaa Leu Leu His Ser Leu Ser Ser Gly Val Arg Ala Pro Ser Pro
  -10 -5 1
- Ala Pro Ser Ser Val Pro Leu Gly Ser Glu Lys Pro Ser Asn Val Ser 5 10 15
- Gln Asp Arg Lys Val Pro Val Pro Ile Gly Thr Glu Arg Ser Ala Arg 20 25 30 35
- Ile Arg Gln Thr Gly Thr Ser Ala Pro Ser Val Ile Gly Ser Asn Leu
  40 45 50
- Ser Thr Ser Val Gly His Ser Gly Ile Trp Ser Phe Glu Gly Ile Gly
  55 60 65
- Gly Asn Gln Asp Lys Val Asp Trp Cys Asn Pro Gly Met Gly Asn Xaa 70 75 80
- Met Ile His Arg Pro Met Ser Asp Pro Gly Val Phe Ser Gln His Gln 85 90 95

Ala Thr Xaa Ala 100

- (2) INFORMATION FOR SEQ ID NO: 313:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 24 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.6

seq PTLCVSSSPALWA/AS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 313:

Met Thr Met Ala Glu Cys Pro Thr Leu Cys Val Ser Ser Pro Ala
-15 -10 -5

Leu Trp Ala Ala Ser Glu Thr Gly
1 5

- (2) INFORMATION FOR SEQ ID NO: 314:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 133 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -25..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.5

seq AQLFACLLRLGTQ/QV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 314:

Met Val Pro Leu Val Ala Val Val Ser Gly Pro Arg Ala Gln Leu Phe
-25 -15 -10

Ala Cys Leu Leu Arg Leu Gly Thr Gln Gln Val Gly Pro Leu Gln Leu
-5 1 5

His Thr Gly Ala Ser His Ala Ala Arg Asn His Tyr Glu Val Leu Val 10 15 20

Leu Gly Gly Ser Gly Gly Ile Thr Met Ala Ala Arg Met Lys Arg
25 30 35

Lys Val Gly Ala Glu Asn Val Ala Ile Val Glu Pro Ser Glu Arg His 40 45 50 55

Phe Tyr Gln Pro Ile Trp Thr Leu Val Gly Ala Gly Ala Lys Gln Leu 60 65 70

Ser Ser Ser Gly Arg Pro Thr Ala Ser Val Ile Pro Ser Gly Val Glu
75 80 85

Trp Ile Lys Ala Arg Val Thr Glu Leu Asn Gln Thr Arg Leu His His
90 95 100

Thr Asp Asp Asp Gly 105

- (2) INFORMATION FOR SEQ ID NO: 315:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 101 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide .
    - (B) LOCATION: -86..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.5

seq ALLTGPTLGSSQA/RW

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 315:

Met Ser Glu Met Ala Glu Leu Ser Glu Leu Tyr Glu Glu Ser Ser Asp
-85 -80 -75

Leu Gln Met Asp Val Met Pro Gly Glu Gly Asp Leu Pro Gln Met Glu
-70 -65 -60 -55

Val Gly Ser Gly Ser Arg Glu Leu Ser Leu Arg Pro Ser Arg Ser Gly
-50 -45 -40

--- 3-- m

Pro Met Ala Xaa Gln Arg Gly Asn Gly Ala Leu Leu Thr Gly Pro Thr
-20 -15 -10

Leu Gly Ser Ser Gln Ala Arg Trp Arg Ala Xaa Thr Ser Arg Ala Arg
-5 1 5 10

Thr Arg Ala Pro Gly
15

- (2) INFORMATION FOR SEQ ID NO: 316:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 37 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.3

seq IVSVLALIPXTTT/LT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 316:

Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Xaa Thr Thr Leu
-15 -5 1

Thr Val Gly Gly Val Phe Ala Xaa Val Thr Ala Val Cys Cys Leu
5 10 15

Ala Asp Gly Gly Gly 20

- (2) INFORMATION FOR SEQ ID NO: 317:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 50 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide

· water

- (B) LOCATION: -29..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5
    seq ELSLLPSSLWVLA/TS
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 317:

Met Thr Cys Arg Gly Ser Cys Ser Tyr Ala Thr Arg Arg Ser Pro Ser
-25 -20 -15

Glu Leu Ser Leu Leu Pro Ser Ser Leu Trp Val Leu Ala Thr Ser Ser
-10 -5 1

Pro Thr Ile Thr Ile Ala Leu Ala Met Ala Ala Gly Asn Leu Cys Pro 5 10 15

Leu Arg 20

- (2) INFORMATION FOR SEQ ID NO: 318:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 58 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - · (A) NAME/KEY: sig\_peptide
      - (B) LOCATION: -15..-1
      - (C) IDENTIFICATION METHOD: Von Heijne matrix
      - (D) OTHER INFORMATION: score 4.9

seq AVVFVFSLLDCCA/LI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 318:

Met Glu Ala Val Val Phe Val Phe Ser Leu Leu Asp Cys Cys Ala Leu
-15 -10 -5 1

Ile Phe Leu Ser Val Tyr Phe Ile Ile Thr Leu Ser Xaa Leu Glu Cys
5 10 15

Asp Tyr Ile Asn Ala Arg Ser Cys Cys Ser Lys Leu Asn Lys Trp Val 20 25 30

. Ile Pro Glu Leu Ile Gly His Thr Ile Gly

(2) INFORMATION FOR SEQ ID NO: 319:

\*\*\*\* T

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 57 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -30..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.9

seq VAHALSLPAQSYG/ND

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 319:

Met Ala Ala Thr Ser Gly Thr Asp Glu Pro Val Ser Gly Glu Leu Val
-30 -25 -20 -15

Ser Val Ala His Ala Leu Ser Leu Pro Ala Gln Ser Tyr Gly Asn Asp

Pro Asp Ile Glu Met Ala Trp Ala Met Arg Ala Met Gln His Ala Glu
5 10 15

Val Tyr Tyr Lys Leu Ile Ser Ser Val 20 25

- (2) INFORMATION FOR SEQ ID NO: 320:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 44 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -17..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.6

seq ALFLLLHNEMVSG/VY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 320:

Met Ala Asp Glu Ala Leu Phe Leu Leu His Asn Glu Met Val Ser

Gly Val Tyr Lys Ser Ala Xaa Xaa Gly Arg Trp Lys Thr Asp Asp Val 1 5 10 15

Leu Leu Ser Trp Lys Thr Trp Gly Phe Glu Trp Asp
20 25

## (2) INFORMATION FOR SEQ ID NO: 321:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 126 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymphocytes
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -119..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.3 seq SVCLSIISMLSSC/KE
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 321:

Met Ala Ser Met Gln Lys Arg Leu Gln Lys Glu Leu Leu Ala Leu Gln
-115 -110 -105

Asn Asp Pro Pro Pro Gly Met Thr Leu Asn Glu Lys Ser Val Gln Asn
-100 -95 -90

Ser Ile Thr Gln Trp Ile Val Asp Met Glu Gly Ala Pro Gly Thr Leu
-85 -80 -75

Tyr Glu Gly Glu Lys Phe Gln Leu Leu Phe Lys Phe Ser Ser Arg Tyr
-70 -65 -60

Pro Phe Asp Ser Pro Gln Val Met Phe Thr Gly Glu Asn Ile Pro Val -55 -45 -40

His Pro His Val Tyr Ser Asn Gly His Ile Cys Leu Ser Ile Leu Thr -35 -30 -25

Glu Asp Trp Ser Pro Ala Leu Ser Val Gln Ser Val Cys Leu Ser Ile
-20
-15
-10

Ile Ser Met Leu Ser Ser Cys Lys Glu Lys Arg Arg Pro Pro
-5
1 5

## (2) INFORMATION FOR SEQ ID NO: 322:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 59 amino acids

--

- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -27..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.1

seq VLMFCVTPPELET/KX

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 322:
- Met Lys Xaa Met Thr Gly Ser Glu Asn Trp Lys Thr Lys Lys Val Leu
  -25 -20 -15
- Met Phe Cys Val Thr Pro Pro Glu Leu Glu Thr Lys Xaa Asn Ile Thr
  -10 -5 1 5
- Lys Gly Gly Leu Val Leu Phe Xaa Ala Asn Ser Asn Ser Ser Cys Met
  10 15 20

Glu Leu Ser Lys Lys Ile Ala Glu Arg Pro Ala 25 30

- (2) INFORMATION FOR SEQ ID NO: 323:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 39 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymphocytes
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -33..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1

seq LFMTRTLCSPGPS/QP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 323:

Met Gln His Ile Val Gly Val Pro His Val Leu Val Arg Arg Gly Leu
-30 -25 -20

Leu Gly Arg Asp Leu Phe Met Thr Arg Thr Leu Cys Ser Pro Gly Pro
-15 -10 -5

· .....

Ser Gln Pro Arg Glu Ala Gly
1 5

- (2) INFORMATION FOR SEQ ID NO: 324:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 68 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8

seq ALALASSQSHLLG/RD

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 324:
- Met Tyr His Gln Ser Glu Ala Leu Ala Leu Ala Ser Ser Gln Ser His
  -15
  -10
  -5
- Leu Leu Gly Arg Asp Ser Pro Ser Ala Val Phe Glu Gln Asp Leu Glu
  1 5 10
- Asn Lys Glu Met Ser Lys Glu Trp Phe Leu Phe Asn Asp Ser Arg Val 15 20 25
- Thr Phe Thr Ser Phe Gln Ser Val Gln Lys Ile Thr Ser Arg Phe Pro 30 35 40 45

Lys Asp Thr Trp

- (2) INFORMATION FOR SEQ ID NO: 325:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 54 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -22..-1

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.8 seq FASVAMICAIASG/SE
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 325:

Met Ser Gly Gln Gly Leu Ala Gly Phe Phe Ala Ser Val Ala Met Ile
-20 -15 -10

Cys Ala Ile Ala Ser Gly Ser Glu Leu Ser Glu Ser Ala Xaa Gly Tyr
-5 1 5 10

Phe Ile Thr Ala Cys Ala Val Ile Ile Leu Thr Ile Ile Cys Tyr Leu
15 20 25

Gly Leu Pro Arg Gln Gly 30

- (2) INFORMATION FOR SEQ ID NO: 326:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 50 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -30..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.7 seq SMMLLTVYGGYLC/SV
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 326:

Met Pro Thr Gly Lys Gln Leu Ala Asp Ile Gly Tyr Lys Thr Phe Ser
-30 -25 -20 -15

Thr Ser Met Met Leu Leu Thr Val Tyr Gly Gly Tyr Leu Cys Ser Val
-10 -5 1

Arg Val Tyr His Tyr Phe Gln Trp Arg Arg Ala Gln Arg Xaa Ala Xaa 5 10 15

Glu Gly 20

- (2) INFORMATION FOR SEQ ID NO: 327:
  - (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -14..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.5

seq FPVCLTVTAAVCG/XX

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 327:

Met Phe Pro Val Cys Leu Thr Val Thr Ala Ala Val Cys Gly Xaa Xaa
-10 -5 1

Ala Gln

- (2) INFORMATION FOR SEQ ID NO: 328:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 49 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.5

seq VIFFACVVRVRDG/LP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 328:

Met Ser Val Ile Phe Phe Ala Cys Val Val Arg Val Arg Asp Gly Leu
-15 -5 1

Pro Leu Ser Ala Ser Thr Asp Phe Tyr His Thr Gln Asp Phe Leu Glu 5 10 15

Trp Arg Arg Leu Lys Ser Leu Ala Leu Arg Leu Ala Gln Tyr Pro 20 25 30

Gly

- Carlotte - Carlotte

## (2) INFORMATION FOR SEQ ID NO: 329:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 89 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymphocytes
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -68..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.5 seq LVLDVVMLLLYLG/IE
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 329:

Met Leu Xaa Gly Gly Leu Lys Met Ala Pro Arg Gly Lys Arg Leu Ser
-65 -60 -55

Ser Thr Pro Leu Glu Ile Leu Phe Phe Leu Asn Gly Trp Tyr Asn Ala
-50 -45 -40

Thr Tyr Phe Leu Leu Glu Leu Phe Ile Phe Leu Tyr Lys Gly Val Leu
-35 -30 -25

Leu Pro Tyr Pro Thr Ala Asn Leu Val Leu Asp Val Val Met Leu Leu -20 -15 -10 -5

Leu Tyr Leu Gly Ile Glu Val Ile Arg Leu Phe Phe Gly Thr Lys Gly
1 5 10

Asn Leu Cys Gln Arg Lys Met Pro Arg 15 20

- (2) INFORMATION FOR SEQ ID NO: 330:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 65 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia -
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -36..-1

· \*\*\*

- · (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.5 seq PALTILHLPGTEG/VA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 330:

Met Ile Gly Gly Gly Arg Trp Asp Pro Pro Gly Ala Gln Ala Pro Ser
-35 -30 -25

Ser Gln Ala Phe Pro Arg Arg Pro Ala Leu Thr Ile Leu His Leu Pro
-20 -15 -10 -5

Gly Thr Glu Gly Val Ala Ser Gln Leu Thr Pro Ala Pro Lys Leu Ser 1 5 10

Ser Ala Ala Gly Trp Leu Glu Val Pro Phe Asp Ala Ile Pro Ala Pro 15 20 25

Gly

- (2) INFORMATION FOR SEQ ID NO: 331:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 57 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Lymph ganglia
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -28..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.4 seq LLRLLCLLPTGLP/VR
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 331:

Met Val Arg Arg Val Gln Pro Asp Arg Lys Gln Leu Pro Leu Val Leu
-25 -20 -15

Leu Arg Leu Leu Cys Leu Leu Pro Thr Gly Leu Pro Val Arg Ser Val

Asp Phe Asn Arg Gly Thr Asp Asn Ile Thr Val Arg Gln Gly Asp Thr 5 10 15 20

Ala Ile Leu Arg Phe Leu Xaa Ser Gly 25

(2) INFORMATION FOR SEQ ID NO: 332:

- MAS -- 25-

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 51 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Lymph ganglia
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -19..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.4

seq LVFIIGLVGNLLA/LV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 332:

Met Pro Leu His Tyr Ser Leu Val Phe Ile Ile Gly Leu Val Gly Asn
-15 -10 -5

Leu Leu Ala Leu Val Val Ile Val Gln Asn Arg Lys Ile Asn Ser 1 5 10

Thr Thr Leu Tyr Ser Thr Asn Leu Val Ile Ser Asp Ile Leu Phe Xaa 15 20 25

Thr Val Gly 30

- (2) INFORMATION FOR SEQ ID NO: 333:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 71 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Umbilical cord
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -30..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.5

seq WATLGLLVAGLGG/HD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 333:

Met Ala Arg Gly Leu Gly Ala Pro His Trp Val Ala Val Gly Leu Leu
-30 -25 -20 -15

Thr Trp Ala Thr Leu Gly Leu Leu Val Ala Gly Leu Gly Gly His Asp
-10 -5 1

Asp Leu His Asp Asp Leu Gln Glu Asp Phe His Gly His Ser His Arg
5 10 15

His Ser His Glu Asp Phe His His Gly Xaa Ser His Ala His Gly His 20 25 30

Gly His Xaa His Glu Ser Met 35 40